The Centers for Disease Control and Prevention

Technologies Brochure

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Contents

BACTERIAL

Bacillus anthracis

A Novel Neutralizing Epitope within *Bacillus anthracis* Protective Antigen

Bacillus anthracis is the gram-positive, spore-producing bacteria responsible for anthrax in humans. Researchers at the CDC have identified a specific range of amino acid sequences in anthrax toxin protective antigen (PA) which is important in anthrax toxin function. Antibodies against this sequence neutralize anthrax toxin activity in cell culture, and can prevent *B. anthracis* infection in animal models. This newly discovered epitope may be developed as all or part of a specific peptide vaccine, and may drive the development of additional reagents to better understand anthrax disease, anthrax toxin activity, and immunization models.

Inventors: Jason Goldstein, Conrad Quinn, Dennis Bagarozzi Jr.
CDC Reference Number: I-025-10

Linear Epitopes of Anthrax Toxin Protective Antigen (PA) for Development of a Peptide Vaccine

Bacillus anthracis is a gram-positive, spore-forming bacteria which causes anthrax in humans. The two known toxins of *B. anthracis* are binary combinations of protective antigen (PA), named for its ability to induce protective immunity against anthrax. The two toxins, edema factor (EF) and lethal factor (LF) can lead to the formation of edema toxin and lethal toxin. Development of a safe and effective vaccine for inhalation and other forms of anthrax infection is imperative, since anthrax can be used in bioterrorism. Current vaccines, while effective, may result in adverse side effects or may require multiple doses. Inventors have identified multiple linear B-epitopes of *B. anthracis* PA and have provided data which makes the basis for developing serologic correlates of protection for PA based vaccines and therapeutics. This may lead to a more effective rPA based vaccine designed for prevention of anthrax using peptide sequences.

Inventors: Vera Semenova, Conrad Quinn, Jan Pohl, Pavel Svoboda
CDC Reference Number: I-003-10

Conjugates of Carbohydrates and Anthrax Protective Antigen

Anthrax, a serious disease with a high fatality rate, is caused by the bacterium *Bacillus anthracis*. This invention provides enhanced synergistic immune response to the Protective Antigen protein (PA) by combining PA with selected carbohydrates. The invention also comprises the method of extraction, purification, and chemical synthesis of the carbohydrate component and the method of combining the PA and carbohydrate. It also describes a novel polysaccharide structure that is present in vegetative cells of *B. anthracis*. This polysaccharide structure is specific to *B. anthracis* and different from that of other closely related Bacillus species. It is a potent antigen and can be conjugated to protein carriers, or chemically synthesized and conjugated to protein carriers, to be used as a vaccine with enhanced immunogenic properties for the prevention of anthrax. In addition, this conjugate may be used as a moiety for distinction of *B. anthracis* from other bacteria, or as a diagnostic tool to detect *B. anthracis* (both spores and vegetative cells) in infected samples.

Inventors: Conrad Quinn, Geert-Jan Boons, Therese Buskas, Alok Mehta, Russell W. Carlson, Elmar Kannenberg, Christine Leoff, Patricia P. Wilkins, Elke Saile
CDC Reference Number: I-024-05, I-52-06

Mass Spectrometry-Based Detection Assay for Anthrax Lethal Factor and Lethal Toxin Activity

This invention identifies an assay for extremely fast and sensitive detection of *Bacillus Anthracis* lethal toxin (LTx), the toxin responsible for the lethal effects of anthrax infection. This assay has already been successfully tested in animals and will allow for early detection of anthrax infection and screening of lethal factors to monitor anthrax infections, such as for vaccine trial candidates. LTx is composed of two proteins, protective antigen (PA) and lethal factor (LF). The assay effectively detects LF by first using magnetic protein G beads to capture and concentrate LF in samples, then testing for LF on the bead by reacting it with a peptide substrate designed to mimic LF's natural target. By testing its reaction to and cleaving of this peptide substrate with mass spectrometry or liquid chromatography, this test can check for LF rapidly and with very high specificity and sensitivity.

Inventors: Anne Boyer, Conrad Quinn, John Barr
CDC Reference Number: I-013-06
Publication Number: WO/2007/136436

FRET-Based Detection Assay for Anthrax Lethal Toxin Activity in Serum

Anthrax is an acute infectious disease caused by the spore-forming bacterium *Bacillus anthracis*. *Bacillus anthracis* produces a highly lethal toxin (LTx) which is a complex of two proteins, protective antigen (PA) and lethal factor (LF). LF is a zinc-dependent endoproteinase that cleaves various response regulators. The CDC has developed an assay that detects LF and LTx in serum which can be used as a rapid, highly sensitive diagnostic test for human exposure to anthrax.

Inventors: Anne E. Boyer, Conrad P. Quinn, John R. Barr
CDC Reference Number: I-027-06

Bordetella pertussis

LC-MS/MS Method for Quatification of Antrax Edema Factor and *Bordetella pertussis* Anylate Cyclase Activity

This is a method to identify and quantify the activity of bacterial adenylate cyclase (AC) toxins by liquid chromotography tandem mass spectrometry (LC-MS/MS). The invention includes detection and quantification of the AC of Bacillus anthracis (anthrax) toxin edema factor. The invention provides a method for rapid diagnosis of anthrax infection in a biological sample.

Inventors: Anne Boyer, Dr. Conrad Quinn, John Barr, Renato Lins, Zsuzsanna Kuklenyik, Maribel Gallegos-Candela
CDC Reference Number: I-017-10

***Bordetella* Specific Capture Reagent**

Pertussis, or whooping cough, is a highly contagious upper respiratory infection. Although it is a vaccine preventable disease, 5000-7000 cases are reported each year in the United States. Current diagnostic approaches identify fewer than 20% of actual cases. This invention captures cells and by-products of the pertussis agents present in clinical specimens from patients. Once captured, the analyte can be detected by different diagnostic technologies. The capture process greatly increases the ability of these tests to diagnose pertussis, leading to more efficacious treatment and interruption of disease transmission.

Inventors: Gary Sanden, Kai-Hui Wu, Pamela Cassiday
CDC Reference Number: I-056-06

Diagnosis of *Bordetella pertussis* (whooping cough) via Nucleic Acid Tests and Diagnostic Algorithm

This invention uses two nucleic acid targets in a polymerase chain reaction assay to better detect *Bordetella pertussis* (whooping) cough. Currently tests diagnose *B. pertussis* less than 20% of the time. The assay of this invention increases the diagnosis rate to over 70% and is able to differentiate between the three types of *Bordetella* infections, thereby distinguishing cases that are preventable by vaccination.

Inventors: Gary Sanden, Kai-Hui Wu, Leonard Mayer
CDC Reference Number: I-023-06

Brucella

Rapid Identification and Discrimination of Brucella Isolates Using Real-Time PCR and High Resolution Melt Analysis

There are seven classic species of Brucella and they can infect a wide range of hosts and have different consequences in each of them. Some species are capable of infecting only animals, while others have the potential to be used as bioterror weapons against humans as well. This invention utilizes high resolution melt analysis to specifically, quickly, and accurately detect and discriminate members of the Brucella genus. The invention also gives scientists the ability to identify novel species that could be further characterized and studied. This assay sets itself apart from the current state of the art by providing an accurate reading and by giving scientists the ability to discriminate between all seven classic Brucella species as well as identify novel species that may emerge.

Inventors: James Winchell, Michael Bowen, Bernard Wolff, Rebekah Tiller
CDC Reference Number: I-001-10

Chlamydia

Real-Time PCR-Based Fluorescent Assay Based on the ompA Gene for Detection of *Chlamydia pneumoniae*

Chlamydia pneumoniae is a ubiquitous pathogen that causes acute respiratory disease and is linked with coronary artery disease, myocardial infarction, carotid artery disease, and cerebrovascular disease. The CDC has developed a real-time polymerase chain reaction assay for the detection of *C. pneumoniae* in humans. This assay utilizes fluorescent technology to provide a reliable, accurate, sensitive diagnostic tool for infection detection directly from clinical samples.

Inventors: Maria-Lucia C. Tondella, Brain P. Holloway
CDC Reference Number: I-042-06

Diagnostic Peptide Sequence Discovered for *Chlamydophilia pneumoniae*

Currently, there are few standardized assays for the detection of *Chlamydophilia pneumoniae* infection of humans. This invention is a peptide sequence that specifically binds *C. pneumoniae* and is recognized by anti-*C. pneumoniae* antibodies. This peptide may be useful for improving diagnostic methods by reducing the variability and high backgrounds found with methods that rely on whole organisms for detection. This peptide may also be useful for production of peptide or DNA vaccines.

Inventors: Eric Marston, Jackie Sampson, Stephen Skelton, George Carlone, Trudy Messmer
CDC Reference Number: I-016-00
Patent Number: 7,223,836

Rapid Method for Molecular Differentiation of Chlamydia Trachomatis Biovars Strains

Infections caused by *Chlamydia trachomatis* are among the most prevalent sexually transmitted diseases in the United States. Infections may lead to pelvic inflammatory disease and infertility. Methods to identify and differentiate molecular types are critical for determining appropriate treatment. Currently, differentiation requires several days. This invention may differentiate *C. trachomatis* biovars in less than an hour while patients are waiting in the clinic.

Inventor: Hsi Liu
CDC Reference Number: I-003-03

Methods and Compositions for the Simultaneous Detection of Multiple Analytes

Epidemiological and vaccine studies of *Streptococcus pneumoniae* and *Chlamydia* require serotype identification. Current methods of serotyping are labor intensive and subjective. This invention utilizes serotype specific antibodies bound to fluorescent beads which allows for simultaneous single tube capture and detection of all *S. pneumoniae* serotypes and three *Chlamydia* serotypes.

Inventors: Melinda Bronsdon, George Carlone, Joseph Martinez
CDC Reference Number: I-009-99
Publication Number: WO/2001/073443

Enterobacteriaceae

Oligonucleotide Probes for Detecting *Enterobacteriaceae* and Quinolone-Resistant *Enterobacteriaceae*

Enterobacteriaceae comprise *Salmonella*, *Shigella*, *Escherichia*, *Klebsiella*, *Enterobactor*, *Serratia*, *Proteus*, *Morganella*, *Providencia*, *Yersinia*, and several less common bacterial genera. These gram negative bacteria cause a wide variety of infectious illnesses. Specific oligonucleotide probes have been developed to be incorporated into methods for the species-specific identification of these *Enterobacteriaceae* in a sample as well as detection and diagnosis of *Enterobacteriaceae* infection in a subject. This invention further provides methods for species-specific identification of these quinolone-resistant *Enterobacteriaceae* as well as the detection and diagnosis thereof.

Inventors: Linda Weigel, Fred Tenover
CDC Reference Number: I-003-98
Patent Number: 6,706,475

Hameophilus Influenzae

Development and Clinical Validation of Three Multiplex Real-Time PCR Assays for Detection of *Neisseria meningitixis* (Nm) *Haemophilus influenzae* (Hi) *Streptococcus pneumoniae* (Sp), and *Neisseria meningitidis* Serogroups

Neisseria meningitidis (Nm), *Haemophilus influenzae* (Hi), and *Streptococcus pneumoniae* (Sp) are bacteria which can cause meningitis or other forms or meningococcal disease, respiratory tract infections, and a wide range of other diseases including pneumonia. This first of these novel assays, NHS, uses primers and probes for detection of Nm, Hi, and Sp in one single reaction. Two more assays, BCY and AXW, use primers and probes to detect Nm serogroups B, C, and Y, and Nm serogroups

A, X, and w135 in one single reaction. These new tests use two primers (forward and reverse) and a TaqMan probe with a specific DNA sequence for PCR-amplification for target genes, leading to improved diagnostic sensitivity and reduced cost and time for lab diagnosis of diseases caused by Nm, Hi, and Sp.

Inventors: Xin Wang, Leonard Mayer, Raydel Mair, M. Jordan Theodore
CDC Reference Number: I-004-11

Real-Time (TaqMan) PCR Assay for Detection for *Haemophilus influenzae* (Hi) Serotype A

Haemophilus influenza is responsible for life-threatening respiratory infections including meningitis. The change in prevalence of disease causing primary serotypes has led to the need for continued monitoring of the detection of serotype replacement and vaccine efficacy. Thus, there is a need for compositions and methods useful to improve detection and serotyping of *H. influenzae*. This assay allows for the detection of the bacterial meningitis pathogen *H. influenzae* serotype A (Hia) in fluid samples, without detecting any of the other serotypes of *H. influenzae*. This invention's utility is found in its ability to identify isolated Hia while maintaining the ability to detect even small numbers of Hia that would be found in clinical specimens.

Inventors: Jennifer Dolan, Cynthia Hatcher, Raydel Mair, Mary Theodore
CDC Reference Number: I-015-10

Pan Real-Time PCR Assays for Detection of *Haemophilus influenzae* (Hi) Including Encapsulated and Non-Encapsulated

Two novel primers and a Taqman® probe hybridizable to conserved sequences on the protein D gene of encapsulated and non-encapsulated strains of *Haemophilus influenzae* (*Hi*) are used in PCR amplification assays to detect the bacteria. The assays provide for improved diagnosis of a variety of *Hi* serotypes and *Hi* related diseases, including non-invasive infections such as otitis media, laryngitis, conjunctivitis, and sinusitis. The assays also improve diagnosis of invasive infections such as bacteremia, pneumonia, and meningitis.

Inventors: Xin Wang, Leanard Mayer, Raydel Mair
CDC Reference Number: I-026-10

Legionella

Real-Time PCR-Based Fluorescent PCR for Detection of *Legionella pneumophila* and *Legionella spp*.

This invention uses fluorescent technology to develop real-time PCR detection of Legionella species. Among the species that this assay can detect are *Legionella spp.* and *Legionella pneumophila*, the bacterium associated with Legionnaires' disease and Pontiac fever**.**

Inventors: Robert F. Benson, Brian P. Holloway, Karen McCaustland
CDC Reference Number: I-026-07, I-041-06

Mycoplasma pneumoniae

Real-Time PCR Multiplex (Four Plex) Assay for Detection of Bacterial Respiratory Pathogens in Clinical Specimens

The invention provides for the simultaneous detection of three atypical bacterial respiratory pathogens (*Mycoplasma pneumoniae*, *Chlamydiophila pneumoniae* and *Legionella spp*) with an internal control testing for the presence of human DNA. The assay tests for all four genetic targets in one reaction and has the potential to test 94 clinical specimens in real time PCR. This invention could potentially become a routine screening test for patients with respiratory illness. No other commercial (four plex) real-time PCR assay is available for three common bacterial respiratory pathogens in clinical specimens.

Inventors: Jonas Winchell, Kathleen Thurman, Agnes Warner
CDC Reference Number: I-030-09

Real-time PCR Assay for the Detection of Mycoplasma-Pneumoniae Using a Cytotoxin Gene Target

This invention is a diagnostic real-time PCR assay to detect the presence of Mycoplasma pneumoniae using a newly discovered toxin gene as a target. M. pneumoniae is the cause of 20-40% of community acquired cases of pneumonia and is particularly severe in children. Diagnosis of M. pneumoniae as the causative agent of pneumonia is very difficult using existing technology and is often unsuccessful due to M. pneumoniae's growth characteristics. Serological detection kits are commercially available but are time consuming, not sensitive, not specific, and require two specimens to make an often subjective and non-definitive diagnosis. This real-time PCR assay would allow for the very specific, rapid diagnosis of M. pneumoniae as the etiologic agent for pneumonia, thus allowing for faster and more appropriate treatment, in addition to providing timely data for a suitable public health response.

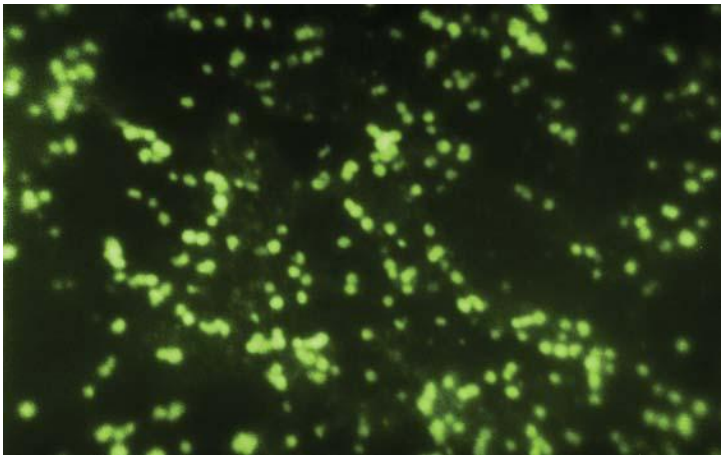
Inventors: Kathleen Thurman, Jonas Winchell
CDC Reference Number: I-022-07

Highly Specific Primers and Probe for Detection *of Mycoplasma pneumoniae* Infection

This invention involves a test for *Mycoplasma pneumoniae* in a real-time PCR-based assay. Currently available assays require a large number of genome copies per sample as well as specific types of test samples that may not be available to the clinic. This CDC assay uses a specific primer sequence and fluorescent-tagged probe sequence to overcome these limitations, and can successfully detect *M. pneumoniae* in respiratory specimens, sputum, tissues of all kinds, serum, whole blood, cerebrospinal fluids, and urine, and can do so with high specificity when as few as 1-5 genome copies per sample are present.

Inventors: Deborah Talkington, Mindy (Ming) Zhang, Brian P. Holloway
CDC Reference Number: I-017-06

Internal Controls and Control Probes for Identifying Inhibitors During Detection Assays of *Mycoplasma Pneumoniae* and *Mycoplasma Fermentans*



This invention covers DNA fragments and fluorescent-tagged probes used to evaluate the presence of inhibitors in PCR-based detection assays of *M. Pneumoniae* or *M. Fermentans*. The internal control probes bind specifically to the internal control DNAs and because of their fluorescence can be distinguished from PCR probes used in the same reaction. Current assays are limited by the required absence of inhibitors that prevent the polymerase in PCR assays from functioning. In the CDC's assay, the probes identify the presence of these inhibitors and thus detect false negative samples that would be reported in other assays.

Inventors: Deborah Talkington, Mindy (Ming) Zhang, Brian Holloway
CDC Reference Number: I-018-06

Neisseria meningitidis

SodC-Based Real-Time (TaqMan) PCR Assay for Detection of *Neisseria meningitis*

Neisseria meningitidis is the etiologic agent of epidemic bacterial meningitis and rapidly fatal sepsis throughout the world. Rapid detection of *N. meningitidis* infection is essential to improved outcomes. At least 16% of carried *N. Meningitidis* lacks the currently used serogroup-based real-time PCR gene target, ctrA. This invention's utility is its ability to detect the bacterial meningitis pathogen *N. meningitidis*, regardless of serogroup. Also, the assay is sensitive enough to detect even the small numbers of *N. meningitidis* that would be found in clinical specimens.

Inventors: Jennifer Dolan, Cynthia Hatcher, Raydel Mair, Mary Theodore
CDC Reference Number: I-016-10

Invasion Associated Genes from *Neisseria meningitidis* Serogroup B

The invention provides nucleic acids and encoded polypeptides associated with invasion of *Neisseria meningitidis*. The polypeptides are used as diagnostic reagents, as immunogenic reagents, and as components of vaccines. The nucleic acids are used as diagnostic reagents, as components of vectors and vaccines, and to encode the polypeptides of the invention. The invention also provides strains of *N. meningitidis* which have an invasion deficient phenotype.

Inventors: Fred Quinn, Nigel Raymond, Efrain Ribot, David Stephens
CDC Reference Number: I-002-95
Patent Number: 6,472,518

Nocardia farcinica

Rapid Identification of *Nocardia farcinica* by a PCR Assay

The bacterial complex *Nocardia* is a serious threat to immunosuppressed individuals, especially those with organ transplants, lung disease, and AIDS. *Nocardia farcinica* is the most clinically significant species because it characteristically demonstrates resistance to multiple, extended spectrum antimicrobial agents. Traditional identification methods are time consuming and labor-intensive (up to 8 weeks for definitive results). This invention comprises a unique DNA sequence within the *N. farcinica* genome which allows for PCR-based diagnostics which are specific to the species and do not cross react with closely related species and genera

Inventors: Brent Lasker, June Brown, Kim Pham
CDC Reference Number: I-027-00
Patent Number: 7,320,881

Streptococcus pneumoniae

Functional Epitopes of *Streptococcus pneumoniae* PsaA Antigen and Uses Thereof

This invention aims to bolster the human body's own mechanisms to fight infection by enhancing an innate immune response, opsonophagocytosis. The specific 24 amino acid sequence (P4) acts as a polymorphonuclear cell activator. P4 can be administered *in vivo* along with a disease's specific antibody to enhance systemic bacterial clearance, thus leading to prolonged survival.

Inventors: Edwin W. Ades,Sandra Steiner, George Carlone, Jacquelyn Sampson, Rajam Gowrisankar, Joseph Matinez, Nikkol Atwell-Melnick, Julie Anderton
CDC Reference Number: I-022-08
Publication Number: WO/2010/014888

Real-Time PCR Primers and Probe for the Detection of *Streptococcus pneumoniae*

This CDC assay improves the TaqMan® real-time PCR assay for the diagnosis of *Streptococcus pneumoniae* from clinical samples. New primer sequences were designed based on a sequence alignment of the lytA gene of *S. pneumoniae* and other related streptococcal species. This invention is aimed at redesigning primers and probes to increase the specificity and sensitivity of the assay for detection of the species.

Inventors: Maria-Lucia C. Tondella, Lesley McGee, Maria Da Gloria Carvalho
CDC Reference Number: I-044-06
Publication Number: WO/2009/011971

Development of Real-time PCR Assay for Detection of Pneumococcal DNA and Diagnosis of Pneumococcal Disease

This invention includes a real-time PCR assay for detecting and diagnosing pneumococcal disease. It will provide a tool for quick and accurate diagnosis by clinicians, and for determining the efficacy of newly licensed polysaccharide-conjugate vaccines or future protein pneumococcal vaccines.

Inventors: Maria Da Gloria Carvalho, Jacquelyn Sampson, Edwin Ades, George Carlone, Richard Facklam, Karen McCaustland
CDC Reference Number: I-001-05
Patent Number: 7,476,733

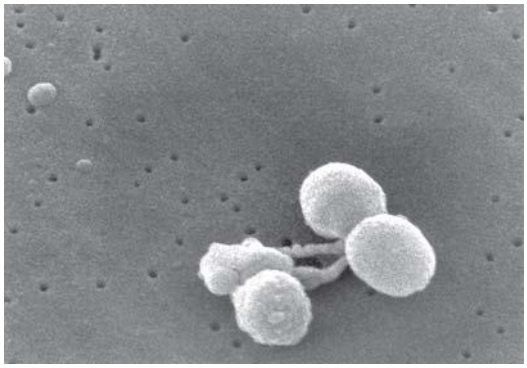
Peptide from *Streptococcus pneumoniae* Surface Adhesion A (PsaA) Protein Associated with Adherence

The invention consists of a P4 peptide which contains functional epitopes of the PsaA protein of *Streptococcus pneumoniae*.. This technology also includes an antibody that can bind to the epitopes of the defined peptides. The technology is a complete kit that includes two vaccines comprised of two separate peptides, a pharmaceutical carrier for each vaccine, methods of using the peptides and antibodies, and diagnostic kits comprising a P4 peptide.

Inventors: Edwin Ades, Jacquelyn Sampson, Sandra Steiner, George Carlone, Joseph Caba, Gowrisankar Rajam
CDC Reference Number: I-030-04
Publication Number: WO/2006/127020

Pneumococcal Fimbrial Protein A

This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.



The present invention relates, in general, to pneumococcal fimbrial protein A. In particular, the present invention relates to a DNA segment encoding a pneumococcal fimbrial protein A gene; polypeptides encoded by said DNA segment, recombinant DNA molecules containing the DNA segment; cells containing the recombinant DNA molecule; a method of producing a pneumococcal fimbrial protein A polypeptide; antibodies specific to pneumococcal fimbrial protein A; and a method of measuring the amount of pneumococcal fimbrial protein A in a sample.

Inventors: Steven O'Connor, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91/0
Patent Number: 5,422,427

Pneumococcal Fimbrial Protein A

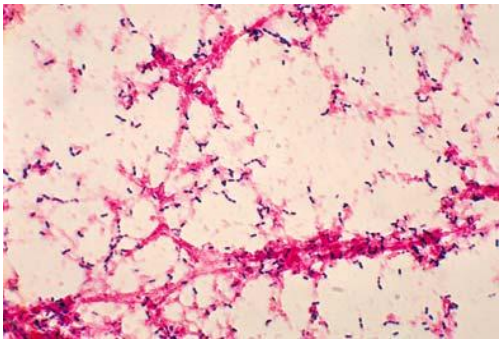
This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.

The present invention relates, in general, to pneumococcal fimbrial protein A. In particular, the present invention relates to a DNA segment encoding a pneumococcal fimbrial protein A gene; polypeptides encoded by said DNA segment, recombinant DNA molecules containing the DNA segment; cells containing the recombinant DNA molecule; a method of producing a pneumococcal fimbrial protein A polypeptide; antibodies specific to pneumococcal fimbrial protein A; and a method of measuring the amount of pneumococcal fimbrial protein A in a sample.

Inventors: Steven O'Connor, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91/3
Patent Number: 6,312,944

***Streptococcus pneumoniae* 37-kDa Surface Adhesin A Protein**

This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.



Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes a pneumococcal protein suitable for vaccine and diagnostic purposes. This invention includes an isolated nucleic acid encoding the 37-kDa protein of S. pneumoniae surface adhesin A, and unique fragments of the nucleic acid encoding the 37-kDa protein of S. pneumoniae surface adhesin A.

Inventors: George Carlone, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91/4
Patent Number: 5,854,416

Streptococcus pneumoniae 37-kDa Surface Adhesin A Protein and Nucleic Acids Coding Therefore

This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.

Disease caused by Streptococcus pneumoniae (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes a pneumococcal protein suitable for vaccine and diagnostic purposes. This invention includes an isolated nucleic acid encoding the 37-kDa protein of S. pneumoniae surface adhesin A, and unique fragments of the nucleic acid encoding the 37-kDa protein of S. pneumoniae surface adhesin A.

Inventors: Jacqueline Sampson, Jean Tharpe, Harold Russell, Edwin Ades, George Carlone
CDC Reference Number: E-157-91/5
Patent Number: 6,217,884

Recombinant Lipidated PsaA Protein, Methods of Preparation and Use

This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.

Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. The present invention relates to recombinant lipidated PsaA proteins and recombinant constructs from which such lipidated PsaA proteins may be expressed. The invention also provides methods of preparation of lipidated PsaA proteins and use of such proteins in immunological compositions. Also provided are vaccines comprising immunogenic lipidated PsaA proteins and methods of use of such vaccines in the prevention and treatment of S. pneumoniae infection.

Inventors: Barun De, Robert Huebner, Jacqueline Sampson, Edwin Ades, George Carlone
CDC Reference Number: I-011-97
Patent Number: 7,635,486

Methods and Compositions for the Simultaneous Detection of Multiple Analytes

Epidemiological and vaccine studies of *Streptococcus pneumoniae* and *Chlamydia* require serotype identification. Current methods of serotyping are labor intensive and subjective. This invention utilizes serotype specific antibodies bound to fluorescent beads which allows for simultaneous single tube capture and detection of all *S. pneumoniae* serotypes and three *Chlamydia* serotypes.

Inventors: Melinda Bronsdon, George Carlone, Joseph Martinez
CDC Reference Number: I-009-99
Patent Number: 7,659,085

Oligonucleotide Sequences for Amplification of _Streptococcus pneumoniae_ Gene

Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. The present invention relates to diagnostic assays and kits for detecting the presence of *S. pneumoniae* in a sample and to vaccines for use against *S. pneumoniae*. More specifically, the invention relates to PCR assays for the presence of *S. pneumoniae* surface adhesion A protein (PsaA) and to vaccines raised against a portion of PsaA encoded by a PCR product that is provided using specific primers.

Inventors: Edwin Ades, Jennifer Crook, Jacqueline Sampson, George Carlone, Katherine Morrison
CDC Reference Number: I-013-99
Patent Number: 6,869,767

Multiple Antigenic Peptides Immunogenic against _Streptococcus pneumoniae_

Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. This invention is an improved peptide construct consisting of a combination of antigenic epitopes of the PsaA (37-kDa) protein from *Streptococcus pneumoniae*. This construct is a possible vaccine candidate which may provide better immune stimulation over vaccines which are based on individual rather than combination epitopes.

Inventors: Danny Jue, Jacqueline Sampson, Scott Johnson, George Carlone, Edwin Ades
CDC Reference Number: I-014-00
Patent Number: 6,903,184 , 7,501,132

Epitope Peptides Immunogenic against *Streptococcus pneumoniae*

Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. This invention describes novel immunogenic peptides obtained from a random library by selection for high affinity binding to monoclonal antibodies specific for PsaA epitopes. In addition, the peptides of the invention have the capability of serving as immunogens in a subject, thereby effectively eliciting the production of antibodies by the subject and additionally conferring protective immunity against infection by *S. pneumoniae*.

Inventors: George Carlone, Maria Westerink, Edwin Ades, Jean Tharpe, Joan Zeiler, Jacqueline Sampson
CDC Reference Number: I-017-97
Publication Number: WO9945121

Multiplexed Pneumococcal Serotyping Assay

This invention comprises a multiplexed screening assay capable of accurately identifying 85-90% of *Pneumococci* serotypes causing disease in the U.S. This assay identifies specific capsular polysaccharides unique to each serotype and provides public health workers with information used for vaccine design, vaccine responses, and trends in pneumococcal disease.

Inventors: Joseph Martinez, George Carlone, Bernard Beall, Terry Thompson
CDC Reference Number: I-001-06

Streptococcus pyogenes

Real-Time Polymerase Chain Reaction for Identification of *Streptococcus pyogenes*

This invention allows identification of *Streptococcus pyogenes* chromosomal DNA from environmental or clinical samples using TaqMan® real-time Polymerase Chain Reaction (PCR) technology. The assay allows identification of the species when no viable organisms are present, for example in clinical samples after antibiotic therapy. When bacteria are present, DNA-based identification of *Streptococcus pyogenes* is potentially easier and cheaper than culture-based methods.

Inventors: Bernard Beall, Antonio L. Gonzalez, Maria Da Gloria Carvalho
CDC Reference Number: I-043-06

Group A Streptococci

Peptide Vaccines against Group A Streptococci

This invention relates to synthetic Group A streptococci (GAS) immunoreactive peptides, compositions comprising the peptide sequences, vaccines, isolated antibodies elicited by the peptides, diagnostic kits comprising the peptides or antibodies, and methods of using the peptides, compositions, vaccines and antibodies. The synthetic peptides of the invention are immunoreactive portions of the M proteins of the most prevalent GAS serotypes in the United States

Inventors: Bernard Beall, George Carlone, Edwin Ades, Jacqueline Sampson
CDC Reference Number: I-039-00
Patent Number: 7,407,664

ENVIRONMENTAL AND AGRICULTURAL

Air Quality

Air Sampler for Collecting Airborne Fungal Spores in a Microcentrifuge Tube for Molecular Analysis

This invention consists of a sampling apparatus that utilizes one or more cyclone separators to collect airborne particles from the atmosphere. The apparatus's function is not only to separate out aerosols from the atmosphere but to also serve as a collection tube for the aerosol particles. Through its unique design the apparatus is able to use the centrifugal force of the air flow on the particles forcing them to separate. Since the sample is collected directly in the collection tube, in situ analysis of the collected particles can be performed. Analysis may include, but is not limited to, PCR, immunoassay analysis, microscopic spore counting, and counting colony-forming units.

Inventors: Teh-hsun "Bean" Chen, Gregory Feather, Jyoti Keswani, Herbert Edgell
CDC Reference Number: I-020-03
Patent Number: 7,370,543

Mold and Fungus

Monoclonal Antibodies against Fungi and Methods for Their Use

Certain fungi found in indoor environments, including homes and businesses, may cause adverse health effects in people and animals by causing infection or provoking allergic reactions. Sick building syndrome, an occupational condition in which workers are sickened by environmental toxins or pathogens, has been associated with the fungus *Stachybotrys chartarum*. This invention provides monoclonal antibodies that can be used to rapidly and accurately test for the presence of fungi in the environment. These antibodies may also be used to assess human exposure to fungi by testing blood and other bodily specimens.

Inventors: Detlef Schmechel, Daniel Lewis
CDC Reference Number: I-002-01
Patent Number: 7,368,256

Pest Control

Mode of Action of Nootkatone, Carvacrol, and Thymoquinone in Arthropods

The exploitation of plants to provide natural, least-toxic pesticides and repellants is a high priority in the combat against vector-borne disease. An evaluation of the pesticide toxicology, insecticidal properties, and the mode of action of nootkatone, carvacrol, and thymoquinone against key arthropod species resulted in the determination that these natural compounds provide an alternate, less-toxic mode of action than existing chemicals currently used in mosquito, tick, and flea control.

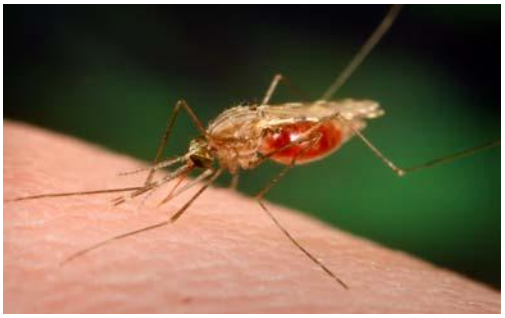
Inventors: Marc Dolan, Joel Coats, Janet Mcallister
CDC Reference Number: I-14-10

A New Device for Collecting Resting Mosquitoes

The device is a small (approximate 1 cubic foot) open-sided container that attracts mosquitoes seeking a daytime resting location. The container is dark-colored and constructed of molded wood-fiber or recycled, high-density plastic. Mosquitoes that enter the dark space of the container are aspirated through a battery-powered fan into a collection receptacle. The receptacle is especially attractive to *Culex* and *Anopheles* mosquitoes, the vectors of the West Nile Virus and malaria parasites, respectively.

Inventors: Nicholas Panella, Rebekah Kent, Nicholas Komar
CDC Reference Number: I-012-09

Compounds for Pest Control and Methods for their Use



The control of public health pests is critical for preventing numerous vector borne diseases throughout the world. New insecticidal compounds and application strategies are needed to protect both public health and the environment, and to combat chemical resistance. In this invention, biologically active fractions of essential oil of Alaska yellow cedar have been identified which are insecticidal and acaricidal. These natural compounds were found to be active for up to 11 weeks against the tick vector, *Ixodes scapularis*; the mosquito vector, *Aedes aegypti*; and the flea vector, *Xenopsylla cheopsis*.

Inventors: Gary Maupin, Joe Karchesy, Nicholas Panella
CDC Reference Number: I-024-00
Patent Number: 7,129,271 , 7,629,387

A Simple Process for Producing Wash-Durable Insecticide Impregnated Bednets or Other Fabrics

In developing countries where diseases such as malaria are prevalent, the use of insecticide impregnated bednets is an effective means for reducing morbidity and mortality of insect borne diseases. However, current procedures for impregnating bednets last only 1-2 washes before re-impregnation is needed. This invention improves the insecticide impregnation process resulting in the production of a bednet that remains sufficiently effective at killing and repelling disease vector mosquitoes/insects after 6-10 washes.

Inventors: Michael Green, Dwight Mount
CDC Reference Number: I-008-99
Patent Number: 6,896,892

Simple, Nondestructive Colorimetric Field Method to Identify and Quantify Cyanopyrethroid Insecticides

This invention encompasses a method to quickly and easily test pyrethroid-impregnated mosquito netting (bednets) for effectiveness. These types of netting are used to combat malarial transmission from disease-transmitting mosquitoes. After extended use or washing, these nets lose the insecticide properties and must be retreated. This simple, nondestructive test reacts to chemicals in the pyrethroid netting treatment to allow field workers to determine a bednet's effectiveness in thirty minutes with an easy to read color change assay.

Inventor: Michael D. Green
CDC Reference Number: I-033-05

Synergistic Combinations of Natural Plant Extracts to Control and Repel Arthropod Pests

There is an increasing need to develop more environmentally friendly insect and tick repellants, or "green" insecticides. The compounds, compositions, and methods that employ a monoterpene carvacrol, used in combination with eremophilane sequiterpenes to control and repel arthropod pests have been evaluated. These natural plant compounds have been demonstrated to be more effective when used in combination than when used individually in laboratory bioassays against ticks, fleas, and mosquitoes. These compounds have minimal adverse effects on humans, animals, and the environment. These compounds may be isolated from natural sources (i.e. Alaska yellow cedar), semi-synthesized from naturally occurring compounds, or completely synthesized. The compounds function as a topical or ingestible toxin and may be applied directly to pests or pest habitats.

Inventors: Marc Dolan, Gary Maupin, Nicholas Panella, Joe Karchesy, EB Gabrielle Dietrich
CDC Reference Number: I-028-04
Patent Number: 7,230,033

MISCELLANEOUS AND METHODOLOGIES

Cell Line

Immortalized Endothelial Cell Line

Endothelial cells are critical components of wound healing, inflammation, circulation, and tumor growth metastases. Endothelial cells are difficult to isolate and culture. A unique approach has been used to immortalize endothelial cells, which are more amenable to culture. The cell line, designated HMEC-1, provides a ready source of human endothelial cells for research, including studies on the physiologic and pathologic factors that induce endothelial mitosis, pharmacological studies for the screening of various agents, and toxicological studies for the cosmetic and pharmaceutical industry.

Inventors: Edwin Ades, Francisco Candal, Thomas Lawley
CDC Reference Number: E-036-91

Food-borne

A Novel Method Developed to Analyze Saxitoxins in Human Urine

This invention describes an analytical method, apparatuses, and compositions for analyzing saxitoxin and neosaxitoxin when secreted in human urine. Saxitoxin and neosaxitoxin are marine toxins consumed in seafood, especially shellfish, and can cause tingling in the lips and extremities, nausea, death via respiratory paralysis. This analytical method, internal standards, developed procedures, and components can be used to assess human exposure to any of the more than fifteen saxitoxins.

Inventors: Rudolph R. Johnson, John R. Barr, Yingtao Zhou, Ernest McGahee, Sherwood Hall
CDC Reference Number: I-061-06

Medical Device

Methods for Controlled Attachment of Bioactive Bacteriophages to Devices for the Purpose of Reducing Pabterial Colonization

Device-associated infections, such as urinary tract infections, cause substantial morbidity and mortality and increase the cost of patient care. These infections are often associated with microbial biofilms that develop on indwelling medical devices. Bacteriophages are self-replicating, self-limiting viruses that infect and kill specific strains of bacteria. This technology provides a controlled method for applying bioactive phages to urinary catheters as well as other biomedical devices by non-covalently associating the phages with a hydrogel coating. These phages are capable of resisting bacterial colonization significantly better than the commercially available hydrogel-coated catheter. This technology could be used to prevent bacteria colonization on the surface of indwelling medical devices such as urinary and intravascular catheters, prosthetic joints, and endotracheal tubes.

Inventors: Dr. Rodney Donlan, Andres Garcia, Susan Lehman
CDC Reference Number: I-019-11

Inactivation of spores and vegetative bacteria on medical devices and instrumentation using elevated pressure carbon dioxide based mixtures.

This invention concerns the use of a flow system where a mixture of an environmentally benign (nontoxic and inflammable) compound in elevated pressure carbon dioxide is effective in sterilization and disinfection of medical devices. Studies have achieved complete sterilization with three different environmentally benign compounds. These mixtures can be used for the disinfection or sterilization of multiple use medical devices, especially for those devices that are made from a polymer material that may react poorly or degrade when other existing methods of sterilization are used. This method may potentially replace current sterilization methods that use hazardous materials.

Inventors: Matthew J. Arduino, Laura Rose, Dennis Hess, Galit Levitin
CDC Reference Number: I-028-07

Method and Apparatus for Cough Sound Analysis

Lung diseases can be differentiated by the location of effect in the lungs which produce variations in cough sounds and patterns. This invention allows subjects to cough into a tubing system allowing the acoustics generated to be recorded with high fidelity and transferred to a computer. Based on these differences, analysis software estimates the lung disease type of the subject. Those who benefit from cough sound analysis include subjects in the early stages of undetected lung disease, subjects with conditions not easily diagnosed by standard techniques, subjects who demonstrate difficulty performing forced expiratory maneuvers and other pulmonary function tests (e.g., elderly, young, and very sick patients), and workers whose respiratory functioning may change during the workday.

Inventors: Walter McKinney, Jeffrey Reynolds, David Frazer, Travis Goldsmith, Aliakbar Afshari, Kimberly Friend
CDC Reference Number: I-020-99
Patent Number: 6,436,057

Auscultatory Training System

This auscultatory training apparatus includes a database of prerecorded physiological sounds (e.g., lung, bowel, or heart sounds) stored on a computer for playback. The program allows a user to select prerecorded sounds for playback. In addition, the program is operable to generate an inverse model of the playback system in the form of a digital filter. The inverse model processes the selected sound to cancel the distortions of the playback system so that the sound is accurately reproduced. The program also permits the extraction of a specific sound component from a prerecorded sound so that only the extracted sound component is audible during playback. As well as a teaching tool to instruct the user on various body sounds, this invention could have applications as a diagnostic screening tool and as a telemedicine tool.

Inventors: Walter McKinney, Jeffrey Reynolds, Travis Goldsmith, Kimberly Friend, David Frazer
CDC Reference Number: I-037-00
Patent Number: 7,209,796

Medical Software

Automated Microscopic Image Acquisition, Compositing, and Display

Micro-Screen is a software program designed to capture images, archive, and display a compiled image(s) from a portion of a microscope slide in real time. This program allows for the recreation of larger images which are constructed from individual microscopic fields captured in up to five focal planes and two magnifications. This program may be especially useful for the creation of data archives for diagnostic and teaching purposes and for tracking histological changes during disease progression.

Inventors: Maribeth Gagnon, Richard Draut, Ed Kurjawski, Roger Taylor, James Lang, Tommy Lee, Carlyn CollinsCDC
Reference Number: I-019-00
Patent Number: 7,027,628
Patent Number: 7,305,109

Finding Usable Portion of Sigmoid Curve

Sigmoid curves are commonly generated in bioassays and used to calculate results. Various techniques have been used to define the curve, analyze the observations, and calculate a concentration. This technology is an algorithmic approach to identifying the usable portion of a sigmoid. . This approach is more objective than other methods, reducing the variability introduced by individuals and/or by repetition and allows substantially higher throughput in a situation where a lot of samples are being analyzed using the same assay.

Inventor: Thomas Taylor
CDC Reference Number: I-019-02
Patent Number: 7,469,186

Methods

Use of Detector Response Curves to Optimize Settings for Matrix Assisted Laser Desorp/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF) MS or Simply (MALDI) and Surface-Enhanced Laser Desorp/Ionization Time-of-Flight Mass Spectrometry (SELDI)

SELDI and MALDI are used for the early detection of diseases such as cervical cancer. This process is known as biomarker discovery. A critical step in this process is the optimization of experiment and machine settings to ensure the best possible reproducibility of results, as measured by the coefficient of variation (CV). The high cost of this procedure includes man hours spent optimizing the machine, opportunity cost, materials used, and spent biological samples used in the optimization process. This technology allows one to characterize the behavior of the CV for a range of machine settings. The technology can be used to optimize the CV with the following advantages over conventional methods: 1) no need to use biological samples, 2) less materials used in the process, 3) improved CV and thus more reproducible results, 4) less man hours required to find good machine settings, and 5) potential full-automation of the process of optimizing CV. This idea is beneficial to all scientists that use MALDI/SELDI for biomarker discovery as well as to manufacturers of MALDI/SELDI.

Inventors: Vincent Emanuele, Brian Gurbaxani
CDC Reference Number: I-001-11

Detection of Activated Antibody-Secreting B-Cells (ASC) as a Method to Diagnose Recent Viral and Bacterial Infections

Individuals who have been vaccinated or naturally infected with mumps can occasionally become re-infected. For these individuals, standard laboratory methods do not work reliably to diagnose the infection. This new technology shows that detection of activated, Antibody-Secreting B-Cells (ASC; or plasmablasts) in the blood can be used to determine if someone has been recently infected with mumps virus. Further, a new ELISpot method for detecting mumps-specific ASC can be adapted to detect cells specific for a wide variety of pathogens including measles, rubella, adenovirus, Epstein-Barr virus (EBV), cytomegalovirus (CMV), paramyxoviruses 1-3, varicella zoster virus (chickenpox), influenza, and pertussis (whooping cough).

Inventors: Donald Latner, Carole Hickman, William Bellini
CDC Reference Number: I-004-10

Simultaneous Measurement of Multiple Drugs Using Fluorescent Covalent Microsphere Immunoassay (FCMIA)

This invention uses a sensitivity enhanced fluorescent covalent microsphere immunoassay (FCMIA) for the rapid, simultaneous, and inexpensive detection of multiple drugs. This technology differs from conventional competitive fluorescent microsphere immunoassay because it is able to simultaneously measure multiple drugs rather than the single measurement of a fluorescent bead bound antibody currently available. This should allow for monitoring of therapeutic drugs in patients to determine optimal doses and determination of drug residues on surfaces to help prevent exposure of workers to those drugs.

Inventors: Jerome P. Smith, Deborah L. Sammons, Shirley A. Robertson
CDC Reference Number: I-025-07

Two Optimized Combination Assays To Examine Apoptosis Pathways in Clinical Samples

This invention consists of two flow cytometric assays that can detect several major aspects of apoptosis. One assay measures caspase-12 activity, the level of active caspase-3, and DNA fragmentation. The second assay assesses depolarization of the mitochondria and phosphatidylserine externalization. These assays have been optimized for use with the low cell numbers and small sample volumes typical of clinical blood samples. These assays can be used to look at various stages and targets of the major pathways of apoptosis, making it possible to understand what points in the apoptosis signaling network are triggered or failing, and can be used to distinguish apoptotic blood cells from non-apoptotic blood cells.

Inventors: Toni Whistler, Mark J. Hollier
CDC Reference Number: I-012-07

Primer Extension Enrichment Reaction (PEER) Protocol

This invention describes a protocol designed to specifically select nucleic acids of very low abundance from a tested specimen or tissue that are not present in a reference specimen.

Inventors: Yuri Khudyakov, Howard A. Fields, Lilia Ganova-Raeva
CDC Reference Number: I-015-02

Microbial Biofilm

Multicoupon Biofilm CFSTR

This device will allow the study of methods to control microbial biofilm formation. The apparatus is used to grow microbial biofilms on multiple, removable substrata for the purpose of determining the effect of selected variables including material of construction, growth medium, and antimicrobial agent concentration, on the growth and activity of biofilm-associated microorganisms.

Inventors: Ricardo Murga, Rodney Donlan, Douglas (Wayne) Kirby
CDC Reference Number: I-006-01

Miscellaneous

Real-time TaqMan® PCR for Human RNaseP Gene

A well characterized, ubiquitous control for use in real-time TaqMan® PCR would benefit researchers performing the procedure. This invention describes the design and optimization of a set of primers and a probe to the human RNaseP gene. The assay can be run as a single assay or in multiplex reactions with samples of human origin that contain genomic DNA or RNA.

Inventors: Karen McCaustland, Brian P. Holloway
CDC Reference Number: I-045-06

Respirable Particle Sampler for the Collection of Air-Borne Fine and Ultrafine Particles Directly Into Surrogate Lung Surfactants for Bioassay

Respirable particulate material such as diesel exhaust frequently contains potential carcinogens. There is a concern that tests conducted using extracts from organic solvents do not provide an accurate representation of the toxicological effects of these compounds on the lung. This invention collects respirable particles directly into the biological surfactant that coats the air spaces of the lung. By preserving particle size and structure for direct bioassay, this sampler simulates the conditions present upon inhalation and deposition in the lung.

Inventors: William Edward Wallace, Jr., Mridul Gautam, Michael J. Keane, Constantinos Sioutas, James Eberhardt, Aleksandar D. Bugarski, Tong-Man Ong
CDC Reference Number: I-031-06

Artificial Human Mutation Controls for Diagnostic Testing

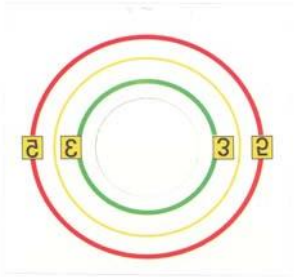
Molecular genetic test development, validation, quality control (QC), quality assurance (QA), and required proficiency testing have historically been hampered by a lack of sufficient positive control material, which generally has been dependent on patient samples donated by laboratories. These samples are often scarce, if available at all, for some genetic tests. The inventors propose a method for synthesizing positive control samples for any genetic disorder for which the coding sequence is known. These are combined with background material in a proprietary formulation to accurately mimic actual samples from patients with the disorder of interest. The technique applied allows for the creation of a permanently transformed control sample with realistic dosing, that accurately mimics the performance of actual patient samples in molecular genetic testing. This technique will enable the synthesis of positive control materials for many molecular genetic tests, and is likely to lead to the development of positive control samples for molecular screening of oncogenes and non-infectious controls for infectious disease testing.

Inventors: Laurina Williams, Wayne Grody, Ramaswamy Iyer, Michael Jarvis
CDC Reference Number: I-007-04
Publication Number: WO/2005/086938

Device to Measure Muscle Contractile/Relaxant and Epithelial Bioelectric Responses of Perfused, Intact Airways *In Vitro*

This device allows, for the first time, measurement of smooth muscle contractile/relaxant activity and transepithelial potential difference (Vt) [or short circuit currents (Isc)] and resistance (Rt) simultaneously in an intact airway in vitro. Investigation of the mechanisms of lung diseases, such as asthma and cystic fibrosis, involves understanding the roles of the airway smooth muscle and epithelium. The smooth muscle is involved in the control of the airway diameter; the epithelium regulates the ionic composition of the liquid lining the airways through electrogenic ion transport and it releases factors that regulate the ability of smooth muscle to contract. The present invention allows simultaneous measurement of smooth muscle contractile/relaxant activity, Vt and Rt under conditions in which the normal spatial relationships between all the cell types are retained and the airway wall is not surgically manipulated or distorted. Because agents can be added separately to the lumen, where they must first cross the epithelium to reach the smooth muscle, or to the outside of the airway, where there is no hindrance of agents to the muscle, the device permits evaluation of functional integrity of the epithelium using pharmacological techniques. It also will permit the effective screening of the effects of agents and drugs on airway epithelium and smooth muscle in the same preparation.
Inventors: Jeffrey Fedan, Yi Jing, Michael Van Scott
CDC Reference Number: I-004-05

Method for Monitoring Local Reaction Associated with Injections



This invention re presents a simple and inexpensive method to give patients a guideline for determining the severity of an adverse reaction that may occur at the site of injection. Patients can be instructed to notify health care providers if an inflammatory response spreads beyond a measured distance from the location of injection.

Inventors: Laurie Kamimoto
CDC Reference Number: I-036-00
Patent Number: 6,833,128

Method for Retaining Methylation Pattern in Globally Amplified DNA

This invention describes a novel method that results in globally amplified DNA copies that retain the methylation signature to make a DNA archive for methylation studies (Meth-DNA archive). Rather than assaying bisulfite-treated DNA directly by PCR or by sequencing methods, a portion is subjected to multiple strand displacement amplification (MDA) using Phi 29 DNA polymerase. MDA results in bisulfite-treated globally amplified DNA (Meth-DNA) retaining the methylation signature present in the original DNA. Aliquots of Meth-DNA archive are used in assays similar to those designed for bisulfite-treated DNA to indicate methylation status of cytosines such as pyrosequencing, methylation specific PCR, or dideoxy sequencing. A Meth-DNA archive is thus created for large scale methylation studies by employing MDA on bisulfite-treated DNA. The novel method described here for creating a Meth-DNA archive should eliminate a significant bottleneck in the collection of methylation information in the genomes of host and pathogens, and thus provide numerous opportunities for the early detection, control and prevention of many chronic and infectious diseases of public health importance.

Inventors: Mangalathu Rajeevan, Elizabeth Unger
CDC Reference Number: I-019-05

PCR Exchangeable Template Reaction

There exists a great need for an efficient means to make synthetic DNA of any desired sequence. Such a method could be universally applied. For example, the method could be used to efficiently make an array of DNA having specific substitutions in a known sequence which are expressed and screened for improved function. The present invention satisfies these needs by providing an efficient and powerful method for the synthesis of DNA. The method is generally referred to as the Exchangeable Template Reaction (ETR) which provides for the synthesis of DNA based on a cyclic mechanism of combining deoxyoligonucleotides. Also included is a series of unique synthesized single-stranded deoxypolynucleotides which can be enzymatically treated to form a unique 3' single-stranded protrusion for selective cyclic hybridization with another unique single-stranded deoxypolynucleotide of the series.

Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: E-184-91
Patent Number: 5,503,995

Methods for the Prevention and Treatment of Diseases Caused by an Inflammatory Response

This invention provides methods for preventing or treating a disease in a subject caused by an inflammatory response to a disease or syndrome that is mediated by endogenous substance P. The methods include administration of anti-substance P antibodies or anti-substance P antibody fragments.

Inventor: Ralph Tripp

CDC Reference Number: I-009-98
Patent Number: 7,101,547

Method for Testing Authenticity of Tamiflu (Oseltamivir)

This invention describes a method to test the authenticity of Tamiflu (Oseltamivir) medication. Because of the popularity and continued effectiveness of this medication in conjunction with the recent outbreaks of avian flu, criminal elements have begun producing and distributing counterfeit versions of Tamiflu to sell to unsuspecting consumers. This invention would provide a simple color-based test for determining a drug's authenticity that could be administered on site by Customs or Border Protection officers and would be a valuable tool in the fight against counterfeit drugs.

Inventor: Michael Green
CDC Reference Number: I-024-06

Use of Cyanidin-3-Glucoside as an Anti-Tumor Treatment

This invention describes the methods of using Cyanid 3 glucoside to treat cancerous tumors. Cyanidin 3 glucoside inhibits neoplastic transformation, metastasis, neoplastic cell migration and invasion, and activation of NF êB, AP 1, COX 2, TNF á and MAPK, and induces apoptosis in neoplastic cell (such as HL 60 cells). Cyanidin 3 glucoside is also demonstrated to possess strong antioxidant activity involving, at least, inhibition reactive oxygen species and induction of cytoprotective genes.

Inventor: Min Ding
CDC Reference Number: I-023-04

Microarray

Integration of Gene Expression Data and Non-Gene Data

Over the last decade, advances in microarray technologies have made gene expression studies increasingly reliable and accessible. These developments have dramatically enhanced the potential for complex gene expression analysis. This invention provides the ability to integrate gene expression data with epidemiologic data. Such analyses can assist in providing diagnostic and prognostic information and profiling disease susceptibility.

Inventors: Suzanne Vernon, Elizabeth Unger, William Reeves, Dan Bui, Stanley Lucas, Amarendra Yavatkar
CDC Reference Number: I-024-02
Publication Number: WO2004050840

Microscope

Improved Compression Algorithm for Images in a Focal Stack

This invention offers a superior method to those currently available for the compression of focal stack images. A focal stack of images is a collection of consecutively focused images from a microscope. Normally, images are compressed individually; this invention takes advantage of images from a collection of focal planes to improve compression.

Inventors: Maribeth Gagnon, Ed Kujawski
CDC Reference Number: I-016-06

Improved Image Acquisition for Bright Field Microscopy

This invention improves the quality of images captured from a bright field microscope using a collection of captured images at different shutter speeds. The technology provides the ability to form a composite image that mimics the image viewed by the human eye.

Inventors: Maribeth Gagnon, Ed Kujawski
CDC Reference Number: I-020-06

Organ Culture

Artificial Organ Culture System

An artificial organ system comprising an artificial microporous membrane with a confluent layer of endothelial cells on one side and a confluent layer of epithelial cells on the other side has been provided. The organ system provided is contained in a vessel. A method for constructing the artificial organ system is also provided. The artificial organ system may be used for studying endothelial passage of pathogens and chemical substances.

Inventors: Fred Quinn, Kristin Birkness, Edwin Ades
CDC Reference Number: E-121-94
Patent Number: 5,695,996

Polymerase Chain Reaction (PCR)

Photoinduced Electron Transfer (PET) Fluorescent Primer for Nucleic Acid Amplification

Researchers are increasingly using fluorescent primers in polymerase chain reaction (PCR) and real-time PCR. Fluorescent primers are useful when used to detect and identify microbes or nucleic acid, amplify nucleic acids for pyro-sequencing and determining the levels of gene expression. However, problems do exist with those current techniques that are used to create fluorescent primers. For one, labeling is not one hundred percent efficient, thus leading to inaccurate results. In addition, it is expensive and time consuming for researchers to make and label their own unique primers. The present invention covers a quick and inexpensive method to make unique fluorescent primers whereby the fluorescent dye attaches to all primers.

Inventors: Vincent R. Hill, Jothikumar Narayanan, Brian P. Holloway
CDC Reference Number: I-060-06
Publication Number: WO/2009/067664

Fluorescent Primer for Nucleic Acid Amplification

Fluorescent chemical-labeled probes and primers are extensively used in clinical and research laboratories for rapid, real-time detection and identification of microbes and genetic sequences. This invention consists of a simple and inexpensive technique for creating fluorescent labeled primers for nucleic acid amplification. During nucleic acid amplification, the "UniFluor" primer is incorporated into newly synthesized double stranded DNA. As a consequence, quenching of the dye's fluorescent signal occurs decreasing the fluorescence of the sample several fold. The decrease in fluorescence can be measured and observed using any commercially available nucleic acid amplification system that measures fluorescence (e.g., "real time" PCR thermocyclers). Since, many real-time PCR applications require a multitude of fluorescently-labeled primers or probes, the single-labeled primer technique also allows researchers and clinicians to perform their work at lower cost.

Inventors: Vincent R. Hill, Jothikumar Narayanan
CDC Reference Number: I-013-04
Patent Number: 20090118490

MYCOBACTERIAL

Tuberculosis

Real-Time Assay to Detect Mycobacterium Tuberculosis Complex and Resistance to Rifampicin and Isoniazsid

Currently, there are few assays available that are capable of both detecting Mycobacterium tuberculosis as well as determining the bacteria's drug resistance. This invention is a real-time PCR assay that is capable of detecting the presence of M. tuberculosis and determining the antibiotic resistance profile to rifampicin and isoniazid. The assay's incorporation of multiple fluorescent chemistries allows for a more cost efficient and less complex method for determining the bacteria's drug resistance.

Inventors: James Posey, Jonas Winchell, Dr. Melissa Ramirez, Kelley Cowart
CDC Reference Number: I-009-10

Identification of M. Tuberculosis Proteins as Mucosal Vaccine Candidates Against TB

This invention involves the identification of preferred dosage and delivery methods for the BCG tuberculosis vaccine. The BCG vaccine uses recombinant protein(s) produced by M. tuberculosis, the bacterium that causes most cases of tuberculosis, in an intranasal vaccine against TB. Intranasal immunization engenders a strong immune response in the lungs, which is beneficial because the M. tuberculosis pathogen primarily gains entry through the respiratory/alveolar mucosa. By stimulating mucosal immunity at the entry site of M. tuberculosis, it is envisioned that this dosage and delivery method for the vaccine would be able to prevent infection and subsequent TB disease.

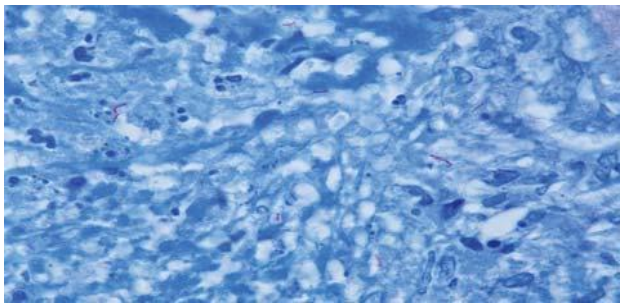
Inventors: Suraj Sable, Thomas Shinnick, Bonnie B. Plikaytis, Mani Cheruvu
CDC Reference Number: I-015-07
Publication Number: WO/2009/089535

SecA Gene of *Mycobacterium tuberculosis* and Related Methods and Compositions

Tuberculosis is a mycobacterial disease which is a major cause of disability and death in the developing world and immunocompromised patients. This invention includes an isolated nucleic acid encoding a SecA protein of *Mycobacteria tuberculosis* and provides methods of screening for putative *M. tuberculosis* virulence factors translocated by the SecA protein. These may further provide for useful vaccines and diagnostic tests for active tuberculosis.

Inventors: Michael Schmidt, Fred Quinn, Marie Owens, Harold King
CDC Reference Number: E-066-95
Patent Number: 5,885,828

A Method for the Rapid Diagnosis of Infectious Disease by Detection and Quantification of Microorganism Induced Cytokines



This invention covers a new method to rapidly and easily detect and quantify cytokines in a patient's blood. Currently available *in vitro* methods to detect latent *Mycobacteria tuberculosis* and other infectious diseases are laborious and expensive because they rely on measuring interferon-gamma response in patient's blood cells. CDC's technology, on the other hand, test detects interferon-gamma and other cytokines using the inherent properties of these molecules in a competitive assay. CDC's new detection method is simpler and easier to perform, thereby rendering new *in vitro* methods faster and less expensive.

Inventors: Gerald "Jerry" Mazurek, Malford E. Cullum
CDC Reference Number: I-038-04

MYCOTIC

Aspergillus

Development and Validation of a Microsphere Luminex-Based Assay for Rapid Detection of Clinically Relevant Aspergillus species

The fungus *Aspergillus* is comprised of approximately 200 types of different molds. *Aspergillus* can often result in several infections with sometimes fatal consequences in immunocompromised individuals such as HIV&AIDS patients or organ transplant recipients. Proper diagnosis is important in effectively treating individuals infected with *Aspergillus*. This Luminex-based assay allows for inexpensive and rapid detection of six different *Aspergillus* species and provides results within five hours of testing, advantageous over the standard culture test which takes between twelve and twenty hours to obtain results.

Inventors: Arunmozhi Balajee, Rui Kano, Kizee Etienne
CDC Reference Number: I-006-08

The Production of Cross-Reactive Monoclonal Antibodies Against *Aspergillus* and *Penicillium* Species

Monoclonal antibodies raised against *Aspergillus versicolor*. These antibodies are not species specific and cross react against multiple *Aspergillus* species and *Penicillium* species.

Inventors: Detlef Schmechel, Daniel Lewis
CDC Reference Number: I-022-03

Detection

Development of DNA Probes to Detect Fungal Pathogens Using a Multi-Analyte Profiling System

Specific DNA probes were developed to identify *Candida* species and endemic mycoses and to differentiate them from other medically important fungi in a multi-analyte profiling system. This system can simultaneously identify up to six different fungi in a single sample and has the potential to identify up to 100 different fungi at once. This method would provide a very rapid and specific diagnosis allowing the administration of appropriate antifungal drug therapy.

Inventors: Christine Morrison, Sanchita Das, Teresa Brown, Brian Holloway
CDC Reference Number: I-022-05
Publication Number: WO/2007/038578

Histoplasma capsulatum

Development of an Antigen-Capture ELISA Using Rabbit Polyclonal Antibody to Detect Histoplasma Capsulatum Antigen in Physiological Specimens

Histoplasmosis is a serious infection that is prevalent is parts of North, Central and South America, particularly in those infected with the HIV virus. It is easily misdiagnosed and thus often incorrectly treated. This invention consists of an enzyme-linked immunosorbent assay (ELISA) for the detection of histoplasmosis in human urine using a rabbit polyclonal antibody to detect the *Histoplasma capsulatum* antigens. This rapid assay expands the detection capability, even in resource-poor countries. Additionally, the polyclonal antibody reagent used in this ELISA could be applied to other assay formats in the future, such as the Western Blot or lateral flow technology.

Inventors: Christina M. Scheel, Mark D. Lindsley, Beatriz Gomez, Sandra Bragg
CDC Reference Number: I-005-09

Nucleic Acids of the M Antigen Gene of *Histoplasma*, Isolated and Recombinant-Produced Antigens, Vaccines and Antibodies, Methods and Kits for Detecting Histoplasmosis

Histoplasmosis is a mycotic infection of varying severity, usually localized in the lungs. Caused by *Histoplasma capsulatum*, infections are usually symptomatic but can develop into chronic disease, especially in immune compromised individuals. The present invention relates to reagents and methods for the detection of histoplasmosis. In particular, the present invention relates to nucleic acids (DNAs) relating to the M antigen gene of *Histoplasma capsulatum*; to vectors and host expression systems containing these nucleic acids; to nucleic acids (RNAs) which encode the M antigen of *H. capsulatum*; to isolated and recombinant-produced antigens encoded by these nucleic acids; to antibodies produced against these antigens; to methods and kits for detecting histoplasmosis using these nucleic acids, antigens and antibodies; and to vaccines for the treatment of prevention histoplasmosis.

Inventors: Timothy Lott, Errol Reiss, Rosely Zancope-Oliveira, George Deepe, Leonard Mayer
CDC Reference Number: I-002-97
Patent Number: 7,018,827

Rapid and Sensitive Method for Detecting *Histoplasma capsulatum*

Histoplasmosis is a mycotic infection of varying severity, usually localized in the lungs. Caused by *Histoplasma capsulatum*, infections are usually symptomatic but can develop into chronic disease, especially in immune compromised individuals. This invention relates to detecting *Histoplasma capsulatum* by PCR using oligonucleotide probes specific for *H. capsulatum*. Test samples may originate from the environment, where *H. capsulatum* spores are found or from clinical samples obtained from patients. Furthermore, the invention also provides for methods that detect the presence of *H. capsulatum* in a sample using a nested, or two-stage, PCR assay.

Inventors: Millie Schafer, Thomas Reid
CDC Reference Number: I-006-97
Patent Number: 6,469,156

Stachybotrys chartarum

Monoclonal Antibodies against Fungi and Methods for Their Use

Certain fungi found in indoor environments, including homes and businesses, may cause adverse health effects in people and animals by causing infection or provoking allergic reactions. Sick building syndrome, an occupational condition in which workers are sickened by environmental toxins or pathogens, has been associated with the fungus *Stachybotrys chartarum*. This invention provides monoclonal antibodies that can be used to rapidly and accurately test for the presence of fungi in the environment. These antibodies may also be used to assess human exposure to fungi by testing blood and other bodily specimens.

Inventors: Detlef Schmechel, Daniel Lewis
CDC Reference Number: I-002-01
Patent Number: 7,368,256

PARASITIC

Cryptosporidium parvum

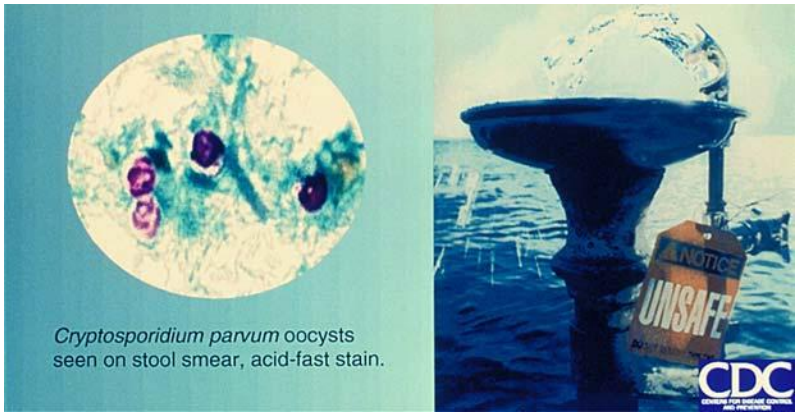
Methods for Detecting *Cryptosporidium parvum* Oocysts

This invention includes methods for detecting parasites, such as *Cryptosporidium parvum*, in turbid and non-turbid samples by solubilizing molecular markers or antigens of the parasite. The molecular markers are solubilized by incubating a sample containing the parasite with a solubilization buffer and detecting the solubilized antigens by electrochemiluminescence. The solubilization buffer contains one or more detergents alone or in combination with one or more denaturing agents in a buffered solution. The methods are an improvement over existing immunofluorescence assays for *C. parvum* because the methods described therein are quantitative, reproducible, have high sensitivity, are not labor-intensive, require only minimal sample processing, and avoid being adversely affected by sample turbidity. In addition, by using an electrochemiluminescence assay, microscopy is not required.

Inventors: Michael Arrowood, Yeuk-Mui Lee, Victor Tsang, Jeffrey Call, Patrick Johnson
CDC Reference Number: I-010-97
Patent Number: 6,475,747

Reagent and Method for Detecting *Cryptosporidium parvum* Oocysts

Cryptosporidium parvum is a parasite which can cause severe diarrhea. It is often spread through contaminated drinking water and unpasteurized juices. Provided are a reagent and method for the specific and highly sensitive detection of *C. parvum* in which the regent is an antibody for a soluble *C. parvum* sporozoite antigen. The assay allows recognition and detection of *C. parvum* in turbid samples. Since there is a lack of crossreactivity with other *Cryptosporidium* species, the assay is also highly specific for *C. parvum* contamination or infection.



Inventors: Long-Ti Xie, Victor Tsang, Kathy Hancock, Jeffrey Call, Michael Arrowood, Yeuk-Mui Lee, Patrick Johnson
CDC Reference Number: I-039-98
Patent Number: 7,410,771

Malaria

Novel Molecular Diagnostic Targets for the Detection of *Plasmodium falciparum* and *Plasmodium vivax*

Polymerase chain reaction (PCR) is a valuable molecular diagnostic technique for detecting malaria parasite species, especially in subclinical and mixed infections. Currently, PCR-based methods for detection of malaria parasite species rely primarily on the 18S rRNA gene target, which has certain limitations in sensitivity and multiplex detection of mixed infections. This new technology describes novel DNA targets for malaria diagnostic application which will improve the molecular diagnosis of malaria. Using these targets, DNA is detectable in concentrations as low as 1 parasite per microliter. The PCR test using these new targets detected *P. vivax* with 98.9% sensitivity and 100% specificity, and *P. falciparum* with 100% sensitivity and 100% specificity in comparison to the standard 18S rRNA gene-based nested PCR.

Inventors: Venkatachalam Udhavakumar, Allison Demas, Naomi Wangui Lucchi
CDC Reference Number: I-024-10

Development of Simple, Filed-Usabel Fluorescence Base LAMP Assay for the Diagnosis of Malaria

Loop Mediated Isothermal Amplification (LAMP) is a recently developed technology for the molecular diagnosis of infectious agents in field settings. This technology has already been adopted for diagnosis of malaria, caused by the parasite *Plasmodium falciparum*. However, inventors have improved this technology by using a portable device to perform molecular diagnosis of malaria, producing a new method that was able to detect *Plasmodium falciparum* samples with 98.9% sensitivity and 100% specificity compared to a standard nested PCR method. This Real-time Fluorescence Loop Mediated Isothermal Amplification (RealAmp) assay can be used for the diagnosis of malaria in point-of-care settings.

Inventors: Venkatachalam Udhavakumar, Allison Demas, Naomi Wangui Lucchi
CDC Reference Number: I-018-10

Colorimetric Assay for Artemisinin Derivatives

This test aims to lessen the anti-malarial drug counterfeiting epidemic by testing for the artemisinin-type drugs, i.e. artemether, artether, and dihydroartmisin through the use of a simple, inexpensive colorimetric test. The test works by indicating the presence or absence of the active ingredient.

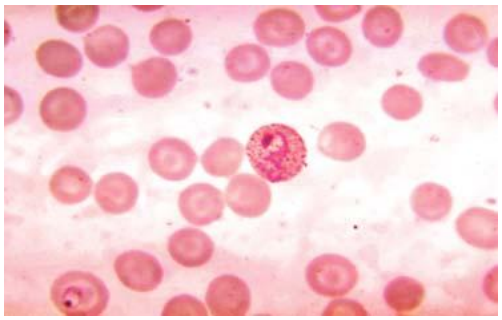
Inventors: Michael Green
CDC Reference Number: I-004-08
Publication Number: WO/2009/061808

Counterfeit Drug Buster

Recent reports have detailed that more than 50% of anti-malarial drugs are counterfeit. The present invention encompasses a device that measures the refractive index of substances. This invention will be of great use in identifying counterfeit drugs to ensure that life-saving therapeutics reach the public.

Inventor: Michael D. Green
CDC Reference Number: I-027-03

Compositions and Methods for Inhibiting Transmission of Malaria



Current malaria vaccine development efforts focus primarily on moderating infection in the human host rather than targeting the mosquito vectors responsible for the spread of malaria. A set of monoclonal antibodies has been developed which inhibit the development of human malaria parasites in different species of mosquitoes by blocking specific mosquito antigens. It may be possible to develop a malaria transmission blocking vaccine by immunizing humans with DNA or protein forms of the identified mosquito antigens. The human antibodies elicited against such antigens, when ingested by the mosquito along with infectious parasites, may prevent the development of parasites in the mosquito and thus halt malaria transmission.

Inventors: Altaf Lal, Pamela Patterson
CDC Reference Number: I-002-00

An Improved Recombinant Multivalent Malarial Vaccine Against Plasmodium Falciparum

The chimeric immunogenic polypeptides comprise peptide eptitopes derived from different stages in the life cycle of the malarial parasite, and, in particular, the *Plasmodium falciparum* parasite. In some embodiments, spacer amino acid sequences are inserted between epitopes. The disclosed chimeric immunogenic polypeptides can be used to stimulate an immune response to the *P. falciparum* parasite in a subject.

Inventors: Altaf Lal, Lihua Xiao, Charles Todd, Paul Schnake, Zhiyong Zhou, Ya Ping Shi, Robert Wohlhueter, Venkatachal Udhayakumar
CDC Reference Number: I-019-03

Recombinant Multivalent Malarial Vaccine against *Plasmodium falciparum*

Malaria continues to be a public health problem throughout the world. *Plasmodium falciparum* is often identified as the cause of the most severe forms of malaria. This invention relates generally to the development and use of a recombinant, multi-valent and multi-stage malaria vaccine and more specifically relates to an antigenic protein useful for preventing or treating *P. falciparum* malarial infections. The invention further provides a vaccine against malaria that is effective in inhibiting reproductive growth of the parasite within a human or animal after initial infection. Also, this invention provides a method for conferring immunity against different stages in the life cycle of the malarial parasite, *P. falciparum*. Furthermore, the invention includes antibodies against a recombinant protein containing antigenic epitopes to various stages of a malarial *Plasmodium* species that may be useful as research or diagnostic reagents for the detection and measurement of *P. falciparum* in a biological sample.

Inventors: Ya Ping Shi, Altaf Lal, Seyed Hasnain
CDC Reference Number: I-004-98
Patent Number: 6,828,416

Taenia solium

Isolation of Diagnostic Glycoproteins to *Taenia solium*, Immunoblot-Assay and Method for the Detection of Human Cysticercosis

Human cysticercosis is a potentially fatal invasion of various tissues by the larvae of *Taenia solium*. The disease has increased dramatically in prominence as a medical problem in the United States since 1977. Increased travel and immigration from highly endemic areas such as Mexico and Central America make recognition and treatment of cysticercosis a U.S. public health priority. This invention is a method and a kit for diagnosing active human neurocysticercosis utilizing an immunoblot assay. This method allows diagnosis of neurocysticercosis by the detection of antigens of larval origin and improves on the specificity and sensitivity of the disc method, achieving 98% sensitivity and 100% specificity. This kit also allows the detection of antibodies in the serum or cerebrospinal fluid.

Inventors: Joy Brand, Anne Boyer, Marianna Wilson, Shirley Maddison, Victor Tsang, Peter Schantz
CDC Reference Number: E-185-88
Patent Number: 5,354,660

Compositions and Methods for Detecting Adult *Taenia solium*

Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasis. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is itself not dangerous, cysticercosis can be fatal. This invention describes adult *T. solium* polypeptides which can be useful as diagnostic agents for the detection of adult tapeworm infection.

Inventors: James Allan, Victor Tsang, Patricia Wilkins
CDC Reference Number: I-028-97
Patent Number: 6,379,906

Methods and Compositions for Detecting Larval Taenia solium with a Cloned Diagnostic Antigen

Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasisis and is acquired by ingestion of *T. solium* cysticerci found in raw and undercooked pork muscle or food contaminated with human or pig feces. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is itself not dangerous, cysticercosis can be fatal. In the present invention, the gp50 antigen has been cloned and may be useful for improvements over the existing Western blot diagnostic method for identifying individuals with cysticercosis.

Inventors: Kathy Hancock, Ryan Greene, Victor Tsang, Patricia Wilkins
CDC Reference Number: I-031-99
Patent Number: 7,094,576, 7,595,059

T24 Antigen for Immunodiagnosis of Taenia Solium Cysticercosis

Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasis. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is itself not dangerous, cysticercosis can be fatal. In order to develop a simple detection assay for field use, the *T. Solium* T24 diagnostic protein was cloned and sequenced.

Inventors: Kathy Hancock, Fatima Williams, Victor Tsang, MelindaYushak, Sowmya Pattabhi
CDC Reference Number: I-009-03
Publication Number: WO/2005/000886

Trichomonas Vaginalis

Efficacy of Dicationic Compounds Against *Trichomonas Vaginalis*

Trichomoniasis has traditionally been treated with 5-nitroimidazole compounds, primarily metronidazole. However, an increasing recognition of *T. vaginalis* isolates that are resistant to metronidazole, combined with a number of individuals who are allergic to this medicine, suggests the need for alternative compounds to treat this infection. The dicationic compounds could fill this need.

Inventors: William Secor, Andrea Crowell, Chad Stephens, David Boykin, Arvind Kumar
CDC Reference Number: I-012-04
Publication Number: WO/2005/086754

RICKETTSIAL

Ehrlichia

Growing Ehrlichia Species in a Continuous Cell Line

Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. In the United States, ehrlichiosis is caused primarily by *E. chaffeensis*. The development of diagnostics and vaccines for these diseases has been hampered by a lack of continuous cell lines to produce large quantities of *Ehrlichia* antigens. In this invention, a method of growing pathogenic *Ehrlichia* species in the continuous monocyte-macrophage cell line DH82 has been developed.
Inventors: Jacqueline Dawson, Yasuko Rikihisa
CDC Reference Number: E-026-90
Patent Number: 5,192,679

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis

Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention includes the new species and an *Ehrlichia chaffeensis* infected cell line deposited with the American Type Culture Collection (ATCC) under accession number CRL 10679.

Inventors: Burt Anderson, Jacqueline Dawson
CDC Reference Number: E-029-91
Patent Number: 5,413,931

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis

Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention includes a PCR based diagnostic kit and methods for diagnosing ehrlichiosis in humans and for screening drugs.

Inventors: Burt Anderson, Jacqueline Dawson
CDC Reference Number: E-029-91
Patent Number: 5,789,176 , 6,541,199

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis

Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention relates to a composition comprising an immunogenic amount of *E. chaffeensis* antigen, either naturally produced or recombinant made, for use in an immunoassay and diagnostic kit.

Inventors: Jacqueline Dawson, Burt Anderson
CDC Reference Number: E-029-91
Patent Number: 6,524,590

Use of Human Immortalized Endothelial Cells to Isolate and Propagate *Ehrlichia chaffeensis* and *Ehrlichia canis*

Ehrlichiosis is non-communicable, rarely fatal disease found in the United States characterized by a sudden onset of fever, chills, malaise and sleeplessness which is related to Sennetsu Fever. Ehrlichiosis is clinically similar to *Rickettsia rickettsii*, Rocky Mountain Spotted Fever, but lacks the distinctive rash. This invention includes a purified immortalized human endothelial cell line infected with *Ehrlichia chaffeensis* or *Ehrlichia canis*.

Inventors: Jacqueline Dawson
CDC Reference Number: E-155-91
Patent Number: 5,401,656

Use of Human Immortalized Endothelial Cells to Isolate and Propagate *Ehrlichia chaffeensis* and *Ehrlichia canis*

Ehrlichiosis is non-communicable, rarely fatal disease found in the United States characterized by a sudden onset of fever, chills, malaise and sleeplessness which is related to Sennetsu Fever. Ehrlichiosis is clinically similar to *Rickettsia rickettsii*, Rocky Mountain Spotted Fever, but lacks the distinctive rash. This invention provides a method for simultaneously screening a human subject for *E. chaffeensis*, *E. canis*, or *Rickettsia rickettsii* by growing the organisms in human microvascular endothelial cells.

Inventors: Jacqueline Dawson
CDC Reference Number: E-155-91
Patent Number: 5,989,848

Novel Granulocytic *Ehrlichia* Genes and Uses Thereof

Granulocytic ehrlichiosis is an acute, potentially fatal tick-borne infection. This invention provides for granulocytic *Ehrlichia* specific genes encoding thirteen proteins that can be used as diagnostic reagents and vaccines. Isolated nucleic acid molecules, purified polypeptides, nucleic acid probes, and antibodies to the thirteen proteins are provided for. The recombinant nucleic acid molecule, vectors, cells and many other forms of the molecule are provided for along with the methods and kit for detection.

Inventors: Cheryl Murphy, Robert Massung
CDC Reference Number: I-011-99
Publication Number: WO0006744

SOFTWARE

Family Healthware - Assessment, Classification, and Intervention Guide

Although family medical history has proven to be an important risk factor for many chronic diseases, it is under-used in the practice of preventive medicine. Existing tools are usually paper-based, time-consuming for the patient, and difficult to interpret for the health care provider. Family Healthware™ is a pc-based familial risk assessment tool. It is a three-step process which uses the disease history of a person's first-and second-degree relatives to assess the risk of common diseases of adulthood and influence early detection and prevention strategies. The risk assessment algorithms that support the tool provide results automatically and take minimal time and effort on the part of the health care provider. A resource manual provides the clinician with updated evidence-based guidelines for disease prevention and screening that are specific to a familial risk.

Inventors: Paula Woon, Maren Scheuner, Muin Khoury, Cynthia Jorgensen
CDC Reference Number: I-004-04
Publication Number: WO/2006/084195

Spatial Random Sampling Using GPS Receivers and Handheld Computers

Sampling is a time consuming task. Not only must researchers obtain samples from numerous locations, but also compile, chart, map and prepare statistical results at their home facility. The present invention relates to software that significantly decreases the time spent in conducting sampling. The software allows researchers to collect and input data while in the field. Moreover, researchers can immediately map spatial points where data was collected. Furthermore, the software allows researchers to immediately access samples and points of sampling in preparing statistical results while in the field. The software works on all handheld computers so long as a GPS receiver is attached. This invention is very useful because it can be used on large scale projects whereby researchers may sample entire villages, towns and cities. Considering this upside, the technology can be applied in numerous settings from conducting surveys to mapping the spread of disease.

Inventors: Anatoly Frolov, Allen Hightower, Adam Wolkon, Jodi L. Vanden Eng
CDC Reference Number: I-047-06

GSA Rent Data Download Tririga Component (Tririga 8i Software Add-on Component)

This Tririga add-on component eliminate several hours of manual data entry and reconciliation tasks each month. This software component streamlines rent collection by downloading monthly rent payment information from the GSA rent invoice website and importing it into Tririga. Downloads can be scheduled and can be performed by month and by specific leases. Rent payment history is maintained and the user can calculate payment projections for future fiscal years.

Inventors: Stanley R. Davis, Lori H. Amos, Ivan J. Dvorak, Allen H. Evans, Jr., Cynthia William
CDC Reference Number: I-029-06

SEXUALLY TRANSMITTED DISEASES

Chlamydia

Methods and Compositions for the Simultaneous Detection of Multiple Analytes

Epidemiological and vaccine studies of *Streptococcus pneumoniae* and *Chlamydia* require serotype identification. Current methods of serotyping are labor intensive and subjective. This invention utilizes serotype specific antibodies bound to fluorescent beads which allows for simultaneous single tube capture and detection of all *S. pneumoniae* serotypes and three *Chlamydia* serotypes.

Inventors: Melinda Bronsdon, George Carlone, Joseph Martinez
CDC Reference Number: I-009-99
Publication Number: WO/2001/073443

Syphilis

Attachment of Cardiolipin to Protein for Development of Non-Treponemal Antibody Assays

This invention comprises a method for reliably attaching cardiolipin to a solid substrate while maintaining its antigenicity, thus being useful for immunoassays for non-treponemal, or anti-lipoidal, antibodies. Currently there are no rapid, on-site immunoassays for non-treponemal antibodies, such as those produced during an immune response from syphilis, partly because the antigens of the non-treponemal antibodies, e.g., cardiolipin, resist attachment to solid supports. Currently available tests require offsite lab work and are expensive to administer. This method overcomes the problems encountered in attaching cardiolipin and other antigens to a solid substrate and would allow the development of a class of strip-based tests (such as nitrocellulose strips) for non-treponemal, or anti-lipoidal, antibodies. This will allow inexpensive and rapid diagnosis of syphilis and most other tissue-damaging diseases.

Inventors: Arnold Castro, Huiying Wang, Robert George, David Cox
CDC Reference Number: I-007-06
Patent Number: WO/2007/061793

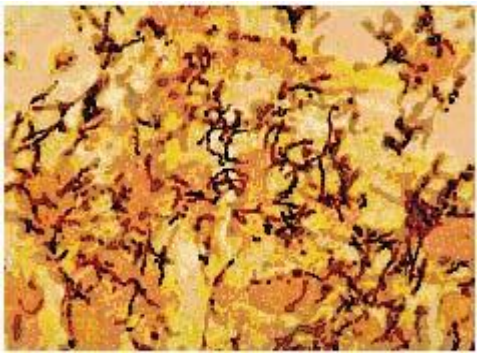
DNA Polymerase from *Treponema pallidum*

This technology has been exclusively licensed for vaccines and is only available for diagnostic purposes.

Syphilis is caused by the spirochete *Treponema pallidum*. This invention provides the nucleic acid and amino acid sequences of the DNA polymerase I region of the *T. pallidum* genome and sequences of nucleic acid molecules that selectively hybridize with nucleic acid molecules encoding the DNA polymerase I enzyme from *T. pallidum* or certain complementary sequences that are described. The nucleic acid molecules are useful for the production of recombinant DNA polymerase I enzyme or as probes to detect the presence of *T. pallidum*. The nucleic acid and amino acid sequences are also useful as laboratory research tools to study the organism and the disease and to develop therapies and treatments for syphilis.

Inventor: Bret Steiner
CDC Reference Number: I-013-96
Patent Number: 6,020,128

Compositions and Methods for Detecting Syphilis Using Synthetic Antigens



Syphilis, a sexually transmitted disease, is caused by *Treponema pallidum*. If left untreated syphilis can cause destruction of the central nervous system and death. In the present invention, an antigen composition and sensitive and specific method for the detection of antibodies to *T. pallidum* are described. The composition is useful as an immunoreagent in immunoassays for the detection of antibodies associated with *T. pallidum* infection.

Inventors: Victoria Pope, William Morrill, Arnold Castro
CDC Reference Number: I-030-98
Patent Number: 6,815,173

Compositions and Methods for Detecting *Treponema pallidum*

Syphilis, a sexually transmitted disease, is caused by *Treponema pallidum*. If left untreated syphilis can cause destruction of the central nervous system and death. Methods for the specific and highly sensitive detection of *T. pallidum* infection comprising the use of specific antigenic proteins and peptides unique to *T. pallidum* are provided. In addition, the methods and compositions of the present invention are directed to the differential detection of specific *Treponema* infections enabling the identification of causative agents for specific *Treponema* disease states: syphilis (*T. pallidum* subspecies pallidum), yaws (*T. pallidum* subspecies pertenue), and bejel (*T. pallidum* subspecies endemicum).

Inventors: Hsi Liu, Bret Steiner, Paul Maddon
CDC Reference Number: I-040-98
Patent Number: 7,335,736

Immunological Immobilization of Cardiolipin Antigen to a Solid Support

This invention comprises a method for immobilizing a lipoidal antigen, comprising cardiolipin, lecithin, and cholesterol, on a solid support (such as a nitrocellulose membrane). The ability to immobilize a lipoidal antigen on a membrane satisfies a long felt need for membrane based assay for the detection of anti lipoidal antibodies.

Inventors: Arnold Castro, Robert George, Victoria Pope
CDC Reference Number: I-010-05
Publication Number: WO/2007/002178

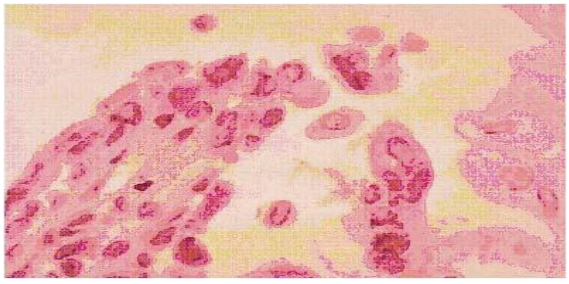
Herpes Virus

Novel Baculovirus Expression Vectors and Recombinant Antigens for Detecting Type-Specific Antibodies to Herpes Simplex Virus

The baculovirus expression vector system was used to express large amounts of herpes simplex virus (HSV) type-specific antigens. The ability to produce large amounts of antigen efficiently should help make accurate, simple, and reliable HSV type-specific serologic assays more widely available. This invention consists of a diagnostic assay for detecting type-specific HSV infection using recombinant baculovirus expressed HSV gG-1 and HSV gG-2 antigens.

Inventors: Demetrio Sanchez-Martinez, Philip Pellett
CDC Reference Number: E-021-91
Patent Number: 6,013,433

Novel Baculovirus Expression Vectors and Recombinant Antigens for Detecting Type-Specific Antibodies to Herpes Simplex Virus



The baculovirus expression vector system was used to express large amounts of herpes simplex virus (HSV) type-specific antigens. The ability to produce large amounts of antigen efficiently should help make accurate, simple, and reliable HSV type-specific serologic assays more widely available. This invention provides novel baculovirus transfer vectors constructed for efficient expression of foreign genes and novel baculoviruses expressing HSV glycoproteins IgG-1 and IgG-2.

Inventors: Philip Pellett, Demetrio Sanchez-Martinez
CDC Reference Number: E-021-91
Patent Number: 6,126,944

VETERINARY

Cat-Scratch Disease

Methods and Compositions for Diagnosing Cat-Scratch Disease and Bacillary Angiomatosis Caused by *Bartonella henselae*

Cat scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat-scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention provides a method of diagnosing cat-scratch disease and bacillary angiomatosis by detecting the presence of *B. henselae* or an immunogenically specific determinant thereof in humans or animals.

Inventors: Burt Anderson, Russell Regnery
CDC Reference Number: E-048-92
Patent Number: 5,399,485 , 5,644,047

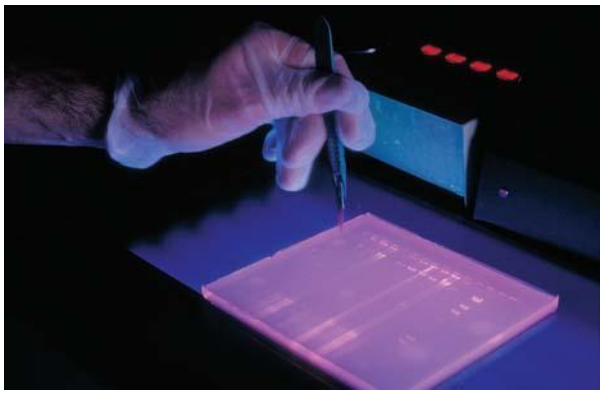
Nucleic Acids Specific for *Bartonella quintana*

Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention provides a method of diagnosing *B. quintana* infection in a subject by detecting the presence of a nucleic acid specific to a purified heat shock protein of *B. quintana*.

Inventors: Russell Regnery, Burt Anderson
CDC Reference Number: E-048-92
Patent Number: 5,693,776

Nucleic Acids of *Bartonella henselae* and Methods and Compositions for Diagnosing *Bartonella henselae* and *Bartonella quintana* Infection

Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention identifies immunogenic peptides useful for identification of *B. henselae* and diagnosis of bacillary angiomatosis.



Inventors: Russell Regnery, Burt Anderson
CDC Reference Number: E-048-92
Patent Number: 5,736,347

Nucleic Acids of *Bartonella henselae* and Compositions for Diagnosing *Bartonella henselae* and *Bartonella quintana* Infection

Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention identifies immunogenic peptides useful for identification of *B. henselae* and diagnosis of bacillary angiomatosis.

Inventors: Burt Anderson, Russell Regnery
CDC Reference Number: E-048-92
Patent Number: 6,406,887

Composition to Protect a Mammal against *Bartonella henselae* Infection

Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention relates to a therapeutic composition to protect a mammal from *B. henselae* infection that includes an isolated *B. henselae* antigen and adjuvant comprising a phosphazene polymer. Also included is a method to use such a therapeutic composition to protect a mammal from *B. henselae* infection. One embodiment is a method to protect a human from cat scratch disease by administering such a therapeutic composition to a domestic cat.

Inventors: Kevin Karem, Russell Regnery
CDC Reference Number: I-007-97
Patent Number: 5,958,414

Canine Influenza

Mouse Monoclonal Antibodies Specific for the H3 Hemagglutinin of Canine Influenza Virus

This invention describes mouse monoclonal antibodies to the H3 hemagglutinin from canine influenza virus, subtype H3N8. Canine influenza, an influenza A virus, was first reported in 2004 and can lead to mild flu-like symptoms or more severe pneumonia-like symptoms in dogs. Because this virus is new to dogs, most dogs will not have a natural immunity to the influenza. The specific H3 hemagglutinin antibodies can be used to develop improved diagnostics and vaccines in order to detect, monitor, and control the spread of canine influenza.

Inventors: Ruben O. Donis, Judith A. Appleton, Lucille F. Gagliardo, Edward J. Dubovi
CDC Reference Number: I-013-07

Chlamydiosis

Genotyping of Chlamydophila psittaci using Real-time PCR and High Resolution Melt analysis

Chlamydophila psittaci is a lethal intracellular bacterial species that causes respiratory problems in humans and avian chlamydiosis in birds. This invention is an assay that detects and genotypes *Chlamydophila psittaci* using Light Upon Extension (LUX) chemistry and High Resolution Melt (HRM) analysis to distinguish the different genotypes of the bacteria. This assay can serve as a potential veterinary diagnostic tool and as a potential pre-screening tool of avian and companion birds. Such applications would result in reduced transmission of the disease to humans.

Inventors: Stephanie Mitchell, Jonas Winchell
CDC Reference Number: I-001-09

Diagnostic Methods

Use of Biotin to Conjugate Antibodies in Serum Samples to Enable Detection of Antigen-specific Antibodies in Species for Which Species-specific Secondary Antibody Conjugates are Commercially Unavailable

This invention enables rapid identification of antigen-specific antibodies in animals when commercial secondary antibody conjugates are not available. The key to this immunoassay is the serum antibody biotinylation method. Biotin, which binds easily to free amines, is used to conjugate serum samples to allow for the detection of antigen-specific antibodies in the serum. The serum thereafter is size-filtered in a 96-well format to remove excess biotin, small proteins and serum components. The biotinylated antibodies are captured in a microsphere immunoassay that uses recombinant West Nile Virus and St. Louis encephalitis virus antigens to bind the antibodies. The captured biotinylated antibodies are detected using strepatividin-phycoerythrin. This format potentially could be used with other etiologic agents of veterinary importance.

Inventors: Alison Jane Johnson
CDC Reference Number: I-027-08

Rabies

Development of Vaccines for the Oral Immunization of Mongoose (Herpestes auropunctatus) against Rabies

This invention is a live, attenuated recombinant rabies virus vaccine that can elicit an effective anti-rabies immune response in wildlife. Innoculation with a live, yet attenuated, virus allows for the production of an antigen in the absence of pathogenicity. Antigenic determinants, which render the rabies virus non-pathogenic, were combined via reverse genetics with determinants that are responsible for elicitation of an immune response. Oral administration of rabies vaccines is preferred because it is most effective in wildlife. Additionally, these vaccines could be used for immunization of stray dogs. More than 90% of human exposures and 99% of human deaths due to rabies worldwide are caused by exposure to rabid dogs, so this vaccine would be very useful in decreasing the transmission of rabies to humans.

Inventors: Charles Rupprecht, Bernhard Dietzschold, Craig D. Hooper, Matthais Schnell
CDC Reference Number: I-034-01
Patent Number: 7,074,413

Raccoon Poxvirus as Gene Expression and Vaccine Vector for Genes of Rabies Virus and Other Organisms

In the United States, the wildlife species most commonly associated with rabies transmission are skunks, raccoons, foxes, and insectivorous bats. Raccoons currently rank second to skunks as the major reservoir. Rabid foxes are a major source of the disease in Canada and many European countries. Although live-attenuated rabies virus vaccines are effective in immunizing foxes against rabies, they are not effective for immunizing skunks and raccoons. An oral rabies recombinant vaccine, based on a putative indigenous raccoon poxvirus, has been developed using raccoon poxvirus as the expression vector. The vaccine confers protection against rabies to a number of wild and domestic animals.

Inventors: Joseph Esposito, George Baer
CDC Reference Number: E-518-87
Patent Number: 5,266,313

VIRAL

Adenovirus

Real-Time TaqMan® PCR for Human Adenovirus Type 4

This invention describes a real-time polymerase chain reaction (PCR) assay using TaqMan® chemistry for detection of human adenovirus type 4 (Had4) genomic DNA in clinical specimens. Unique oligonucleotide primer and probes are used to target regions of the Had4 hexon protein gene. This CDC assay can be used to diagnose acute respiratory illness and can facilitate surveillance testing for pandemic influenza.

Inventors: Dean D. Erdman, Xiaoyan Lu
CDC Reference Number: I-035-06

Astrovirus

Astrovirus VA1: a Novel Astrovirus

Astroviruses are known to infect a variety of mammalian species and typically cause diarrhea. Diarrhea causes an estimated 1.8 million deaths worldwide annually as it is one of the leading infectious causes of death worldwide, with children in developing countries bearing most of the disease burden. This discovery introduces a new virus, Astrovirus VA1 that could be shown to be a major cause of diarrhea outbreaks in future studies. Furthermore, it provides means to diagnose, treat, and prevent this condition. The sequence of this astrovirus is highly divergent from previously described viruses. Reagents based on this new virus could be used to identify the public health significance of this virus in humans. Astrovirus VA1 is responsible for a portion of the 40% of diarrheal disease that cannot be explained by known microbial agents. Identifying causes of diarrheal disease is an essential step in eventually being able to develop therapeutics to treat or vaccines to prevent this condition.

Inventors: Jan Vinje, Suxiang Tong, Yan Li
CDC Reference Number: I-20-09

Nucleic Acids Encoding Human Astrovirus Serotype 2 and Uses Thereof

Astroviruses are a cause of acute gastroenteritis in children and adults worldwide. The present invention provides a nucleic acid encoding human astrovirus serotype 2, or a unique fragment thereof. The sequence, a genomic RNA of human astrovirus serotype 2, contains 6,797 nucleotides, and is organized into three open reading frames. Also provided are purified antigenic polypeptide fragments encoded by the nucleic acid encoding human astrovirus serotype 2, or unique portions thereof. The sequence information of the present invention can be used to detect astroviruses in clinical specimens by utilizing PCR techniques. Additionally, the sequence data can be used to generate recombinant microorganisms expressing astrovirus capsid proteins and, subsequently, can be used to produce antigens for diagnosis of astrovirus infection.

Inventors: Roger Glass, Baoming Jiang, Stephen Monroe, Marion Koopmans
CDC Reference Number: E-059-93
Patent Number: 5,625,049

Bocavirus

Real Time TaqMan PCR Assays and Positive Control for Human Bocavirus

There have been few reports on the epidemiology, geographic distribution or clinical features of human Bocavirus (HBoV) infection. Using Real-Time Taqman® PCR and by targeting the HBoV NS1 and NP-1 genes, this CDC assay provides sensitive, specific and quantitative detection of HBoV in patients with respiratory illness.

Inventors: Dean D. Erdman, Xiaoyan Lu
CDC Reference Number: I-046-06

Ebola

Vaccination Method to Protect Against Ebola Virus

Outbreaks of hemorrhagic fever caused by Ebola virus are associated with high mortality rates. The rapid progression of the virus allows little opportunity to develop natural immunity, and there is currently no effective anti-viral therapy. Therefore, vaccination offers a promising intervention to prevent infection and limit spread. This invention describes a highly effective vaccine strategy for Ebola virus infection in primates. The strategy entails a combination of DNA immunization and boosting with adenoviral vectors that encode viral proteins, and has been shown to generate cellular and humoral immunity in cynomolgus macaques. This invention demonstrates that it is possible to develop a preventive vaccine against Ebola virus infection in primates.

Inventors: Anthony Sanchez, Zhi-Yong Yang, Nancy J. Sullivan, Gary J. Nabel
CDC Reference Number: I-035-97
Publication Number: WO/2003/028632

Immunization for Ebola Virus Infection

This invention concerns nucleic acid molecules that encode Ebola viral proteins, including the viral nucleoprotein, and the transmembrane and secreted forms of the viral glycoprotein, to be use in a vaccine designed to prevent Ebola virus infection. This invention also describes a method for administering an effective amount of Ebola virus vaccine in order to immunize a subject against Ebola virus infection. An effective vaccine is necessary because of the rapid progression of Ebola hemorrhagic fever, which allows little opportunity to develop natural immunity, and the lack of an effective anti-viral therapy.

Inventors: Anthony Sanchez, Gary J. Nabel
CDC Reference Number: I-036-97
Patent Number: 6,852,324

Mutant Form of Ebola Virus - Pseudotyped Retrovirus Vectors

A modified glycoprotein has been developed with an improved affinity for mammalian cell surface receptors over the wild-type form. This new glycoprotein facilitates specific binding to cells and also acts to promote the entry of pseudotyped virus particles into the cytoplasm of cells. This invention not only can be an important tool in the area of pseudotype virus gene therapy, but also in molecular biology research for inserting sequences into target cells.

Inventors: Anthony Sanchez, David A. Sanders, Scott A. Jeffers
CDC Reference Number: I-035-02
Publication Number: WO/2003/102219

Recombinant Infectious Molecular Clone of a Simian Foamy Virus (SFV) Expressing a Truncated form of the Ebola Virus Glycoprotein Gene

This invention involves the engineering of recombinant Simian Foamy Virus SFV (pFOV-7) which may be used to produce a vaccine against Ebola virus infection. The engineered SFV elicits a protective immune response in the host by expressing a truncated Ebola virus gp gene (EbGP) as a fusion protein with SFV. This vaccine can be used by those at risk in endemic areas and by health professionals investigating outbreaks and treating patients. It may also as a vaccine to be used in the event an Ebola virus is used as a biological weapon.

Inventors: Thomas Folks, Anthony Sanchez, James Smith
CDC Reference Number: I-003-06

Enterovirus

Detection and Identification of Nonpolio Enteroviruses

Enteroviruses are one of the most common viruses infecting humans, causing illnesses ranging from mild (e.g., hand-foot-and-mouth disease and acute hemorrhagic conjunctivitis) to more serious disease (e.g., meningitis, paralysis, and encephalitis). Currently, no molecular reagents can distinguish between the 60+ enterovirus serotypes. CDC scientists developed this method to produce PCR primers capable of differentiating the 60+ serotypes of nonpolio enteroviruses (NPEVs).

Inventors: David Kilpatrick
CDC Reference Number: I-001-96
Patent Number: 6,168,917

Typing of Human Nonpolio Enteroviruses

Enteroviruses infect 30-50 million Americans each year, resulting in 30-50,000 hospitalization for aseptic meningitis, as well as cases of acute flaccid paralysis, encephalitis, neonatal sepsis-like disease, and other illnesses. This invention provides a method for the rapid serotype identification of human enteroviruses, reducing the time required for typing from weeks to a few days. Application of the method will also provide data that may be useful for the development of additional virus-specific diagnostic reagents.

Inventors: Mark Pallansch, Kaija Maher, Steven Oberste, David Kilpatrick
CDC Reference Number: I-028-98
Patent Number: 6,846,621

Sensitive, Semi-nested PCR-Amplification of VP1 Sequences for Direct Identification of Enteroviruses Serotypes from Orical Specimens

A reverse transcription/semi-nested polymerase chain reaction (RT-snPCR) assay was developed for detection and identification of enterovirus (EV) RNA in clinical specimens. The primers were designed for broad specificity and amplified all recognized and proposed EV serotypes and other antigenic variant strains tested. PCR products were successfully amplified and sequenced from cerebrospinal fluid, nasopharyngeal swabs, eye swabs, rectal swabs, and stool suspensions, allowing unambiguous identification of the infecting virus in all cases. The VP1 sequences derived from RT-scPCR products allow rapid phylonos.

Inventors: William Nix, Steven Oberste
CDC Reference Number: I-016-05
Patent Number: 7,247,457

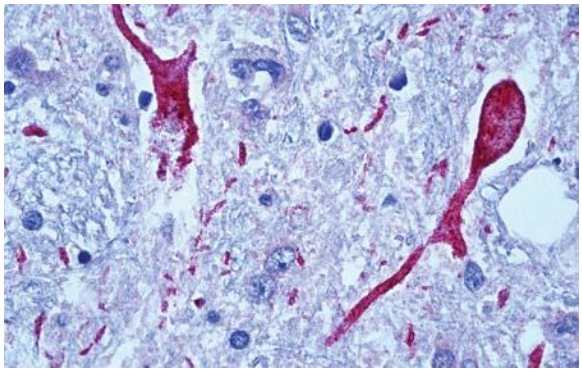
Flavivirus

Vitronectin as a Biomarker for the Detection of a Severe Dengue Infection

Proteomics studies the role of proteins in healthy and disease states, and can be used to complement existing genetic analysis. Biological material such as serum, whole blood, tissue, saliva, urine, and other excreted fluids can be analyzed for unique biomarkers that could designate a disease state versus a healthy state of an individual. CDC Researchers used current proteomics methods, including a new mass spectrometry called surface enhanced laser desorption/ionization-time of flight mass spectrometry (SELDI-ToF), to identify host biomarkers for dengue fever (DF) and dengue hemorrhagic fever (DHF). Using this technique, vitronectin, a major cell adhesion protein found in the plasma and the liver, was identified as an important biomarker for identification of DHF disease state. Vitronectin levels may be used as a specific marker for DHF during the acute phase of the disease.

Inventors: Elizabeth Hunsperger, Momar Ndao, Kay Tomashek, B. Katherine Pool-Smith
CDC Reference Number: I-013-11

Nucleic Acid Vaccines for Prevention of Flavivirus Infection



Mosquito borne viral encephalitis is often caused by a flavivirus such as Japanese encephalitis virus (JEV) or West Nile virus (WNV). This novel vaccine for flaviviruses comprises recombinant nucleic acids that contain genes for structural proteins of flaviviruses, such as JEV. These vaccines serve as a transcriptional unit for the biosynthesis of the virus protein antigens when administered in vivo. Furthermore, the invention provides for a method of immunizing a subject against infection by a flavivirus.

Inventor: Gwong-Jen Chang
CDC Reference Number: I-008-97
Patent Number: 7,417,136

Nucleic Acid Vaccines for Prevention of Flavivirus Infection

The present invention encompasses isolated nucleic acids containing transcriptional units which encode a signal sequence of one flavivirus and an immunogenic flavivirus antigen of a second flavivirus or of a chimeric immunogenic flavivirus antigen comprising sequence from more than one flavivirus. The invention further encompasses a nucleic acid and protein vaccine and the use of the vaccine to immunize a subject against flavivirus infection. The invention also provides antigens encoded by nucleic acids of the invention, antibodies elicited in response to the antigens and use of the antigens and/or antibodies in detecting flavivirus or diagnosing flavivirus infection.

Inventors: Gwong-Jen Chang
CDC Reference Number: I-001-01
Publication Number: WO02081754
Patent Number: 7,521,177 , 7,632,510 , 7,662,394

Hantavirus

Nucleic Acid of a Novel Hantavirus and Reagents for Detection and Prevention of Infection

An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. The Sin Nombre strain identified in this invention (previously termed Four Corners virus) is the etiologic agent responsible for the outbreak of the adult respiratory distress syndrome (ARDS) in the Four Corners region of the United States. Hantavirus strains found in the southwestern U.S. are now known to be primarily the Sin Nombre strain of the virus.

Inventors: Thomas Ksiazek, Stuart Nichol, Christina Spiropoulou, Pierre Rollin
CDC Reference Number: E-183-93
Patent Number: 6,620,913

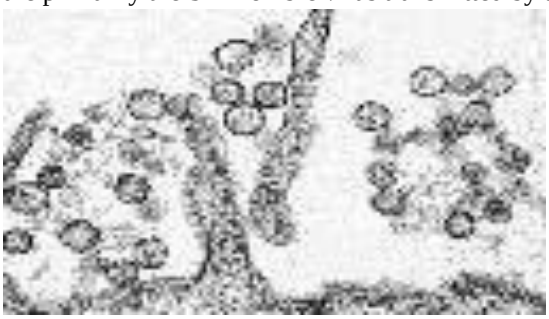
Nucleic Acids of a Novel Hantavirus and Reagents for Detection and Prevention of Infection

An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. The Sin Nombre strain (previously termed Four Corners virus) is the etiologic agent responsible for the outbreak of the adult respiratory distress syndrome (ARDS) in the Four Corners region of the United States. This invention includes nucleic acids of this newly discovered virus and nucleic acid reagents for use in methods of detection and prevention of infection by the virus.

Inventors: Stuart Nichol, Pierre Rollin, Christina Spiropoulou, Thomas Ksiazek
CDC Reference Number: E-183-93
Patent Number: 5,945,277

Black Creek Canal Hantavirus and Related Methods

An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. Hantavirus strains found in the southwestern U.S. are primarily the Sin Nombre virus transmitted by the deer mouse. A previously unreported species of hantavirus is the causative agent of an outbreak in Florida. The virus responsible for this occurrence was isolated from cotton rats and represents a new and distinct serotype of hantavirus and is designated the Black Creek Canal hantavirus. This invention includes nucleic acids and antibodies for use in methods of detection and prevention of infection by the new virus.



Inventors: Sergey Morzunov, Thomas Ksiazek, Stuart Nichol, Pierre Rollin, Eugeny Ravkov
CDC Reference Number: E-183-93
Patent Number: 5,853,980

Bayou Hantavirus and Related Methods

The present invention relates to the discovery and isolation of a novel hantavirus designated the Bayou hantavirus. In particular, the present invention relates to nucleic acids of the newly discovered virus and to nucleic acid reagents (primers and probes), purified polypeptides and antibodies for use in methods of detection and prevention of infection by the virus. A vaccine or purified immunogenic polypeptide of the Bayou hantavirus in a pharmaceutically acceptable carrier is provided. A vector comprising the nucleic acids of the invention is provided. A method of detecting the presence of a hantavirus in a subject comprising contacting an antibody-containing sample from the subject with a purified polypeptide of the invention and detecting the reaction of the polypeptide and the antibody is provided. A method of detecting the presence of the Bayou hantavirus is provided comprising reverse transcribing viral RNA to synthesize a complementary DNA sequence followed by amplifying the DNA using primers which are selective for the Bayou hantavirus and detecting the presence of amplification, thereby indicating presence of the Bayou hantavirus in the sample.

Inventors: Pierre Rollin, Sergey Morzunov, Stuart Nichol, Thomas Ksiazek, Christina Spiropoulou
CDC Reference Number: E-183-93
Patent Number: 5,916,754

Hepatitis

Systemically Delivered Nano-immunolipoplex Vaccine for Prevention/Therapy of Hepatitis C Virus (HCV)

There is currently no vaccine for hepatitis C virus (HCV). This CDC vaccine has the potential to prevent viral replication and improve the efficacy and speed of the T cell response by stimulating the immune response at the liver, the primary site of replication of HCV. The vaccine involves priming with DNA plasmid expressing nonstructural proteins of HCV followed by a boosting with a recombinan, adenovirus.

Inventors: Krysztof Z. Krawczynski, Stephen M. Feinstone, Marian Major, Esther Chang
CDC Reference Number: I-032-06

Antigenically Reactive Regions of the Hepatitis A Virus Polyprotein

Hepatitis A (HAV) causes a transient illness, easily spread through contaminated water and food. While HAV infection is vaccine preventable, administration of the vaccine is usually restricted to epidemics and persons at increased risk. Vaccination in endemic countries may be inadequate. This invention provides for isolated, immunogenic HAV peptides corresponding to immunogenic epitopes of HAV. Moreover, various specific diagnostic embodiments utilizing these new discoveries are also disclosed.

Inventors: Howard Fields, Yuri Khudyakov
CDC Reference Number: I-005-96
Patent Number: 6,838,237

Neutralizing Immunogenic Hepatitis E Virus Polypeptides

Hepatitis E virus (HEV) is a recently discovered agent of enterically transmitted non-A, non-B hepatitis (ET-NANB). The disease remains a serious problem in many developing countries. Unlike other agents of viral hepatitis, HEV infection is often associated with high mortality rates in infected pregnant women. This recombinant protein is being utilized as a diagnostic reagent in the development of immunoassays for the detection of anti-HEV activity in human sera. This protein may also have potential for use as a vaccine to prevent HEV infection.

Inventors: Howard Fields, Yury Khudyakov, Jihong Meng
CDC Reference Number: I-013-00
Patent Number: WO/2001/077156

Synthetic Peptides Immunoreactive with Hepatitis A Virus Antibodies

Hepatitis A (HAV) virus causes a transient illness, easily spread through contaminated water and food. While HAV infection is vaccine preventable, administration of the vaccine is usually restricted to epidemics and persons at increased risk. Vaccination in endemic countries may be inadequate. In this invention synthetic peptides immunoreactive with HAV antibodies have been developed. The peptides are useful as laboratory reagents to detect or quantify HAV antibodies in biological samples, in clinical or research-based assays and for inducing an immune response to HAV when administered to a human or animal. The peptides contain antigenic epitopes, modified antigenic epitopes or combinations of epitopes of the major structural capsid polypeptides or non-structural polypeptides of HAV and contain one or more molecules of the amino acid glutamine at the carboxyl end of the peptide, which enhances immunoreactivity and immunogenicity, particularly IgM antibody reactivity.

Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: I-015-98
Patent Number: 7,223,535

Mosaic Protein and Restriction Endonuclease Assisted Ligation Method for Making the Same

This invention consists of a mosaic protein comprising a variety of immunoreactive antigenic epitopes from several genotypes of hepatitis C virus. The mosaic protein provides a sensitive and specific immunological hepatitis detection assay. A restriction enzyme assisted ligation method of making an artificial gene permits controlled construction of mosaic proteins, and allows confirmatory expression of the intermediate gene products.

Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: I-018-97
Patent Number: 6,030,771

Antigenic Epitopes and Mosaic Polypeptides of Hepatitis C Virus Protein

Hepatitis C (HCV) virus has emerged as a significant public health problem due to widespread infection from blood transfusions given prior to the availability of routine screening. It also continues to be a significant problem in countries with substandard health care practices. This invention comprises a single artificial gene composed of immunodominant epitopes. The expressed protein has significant diagnostic relevance for the detection of antibodies to HCV. Accordingly, this invention is useful as reagents for the diagnosis or monitoring of HCV in a biological sample. These epitopes and polypeptides are also useful for the construction of immunogenic pharmaceutical compositions such as vaccines.

Inventors: Howard A Fields, Yuri Khudyakov
CDC Reference Number: I-022-98
Patent Number: 7,052,696

HIV and Retroviruses

Development of a New One-Well Limiting-Antigen Avidity Enzyme Immunoassay (Lag Avidity-EIA) to Detect Recent HIV-1 Infection Using a Multi-Subtype Recombinant Protein, rIDR-M

Surveillance of HIV-1 provides information on prevalence rates of the disease but determination of new infection rates (HIV-1 incidence) is difficult to deduce. Longitudinal follow up is expensive and can be biased. This new Limiting-Antigen Avidity Enzyme Immunoassay (LAg-avidity-EIA) provides an easy way to measure increasing binding strength (avidity) of HIV antibodies as part of maturation HIV antibodies after seroconversion, providing a method to distinguish early from long-term HIV-1 infection. Unlike current assays which use antigens derived from only one subtype and use two wells, this new assay uses a multi-subtype recombinant protein to permit equivalent detection of antibody avidity among different subtypes, and measures binding strength of antibody in one well. This new assay will allow testing of more specimens and better reproducibility due to its design; it is likely to be more robust and provide more accurate results. The assay may be used for individual diagnosis of recent or long-term infection, but also can be an important tool for surveillance worldwide for assessing trends of new infections and monitoring success of prevention efforts by major public health agencies.

Inventor: Bharat Parekh
CDC Reference Number: I-027-09

Multivalent Multiple-Antigenic-Peptides (MAPs) for the Detection of Antibodies to HIV-1 Group M, N, and O, and HIV-2

HIV is divided into two types: HIV-1 and HIV-2. HIV-1 is further subdivided into group M, N, and O, while HIV-2 is subdivided into subtype A and B. Within HIV-1 group M, 9 different subtypes and numerous forms of recombinant viruses exist. A mixture of antigens derived from different viral strains representing different HIV types and subtypes is needed to detect all types, groups, and subtypes of HIV by serological methods. However, within this mixture, the competition and dilution effect lead to a reduction in assay sensitivity. This new invention includes multivalent multiple-antigenic-peptides

(MAPs) which contain multiple branches of oligopeptides of different sequences. Thus, a single MAP can be used to detect HIV-1 group M alone, HIV-2 alone, or to simultaneously detect HIV-1 groups M, N, O, and HIV-2 with high sensitivity and specificity.

Inventors: Chou-Pong Pau
CDC Reference Number: I-024-09

Development of a Rapid Assay for the Extraction, Amplification and Detection of Human Immunodeficiency Virus Nucleic Acid

This invention provides a quick, inexpensive and technically facile method to detect HIV infection. This microfluidic device quantitatively measures HIV RNA, thus providing a method to measure virus load as well as antiviral therapeutic efficacy. The device requires minimal training for proper use and can detect the virus within thirty minutes from a single sample. This technology could also be use to detect other infectious diseases with the same sample.

Inventors: Timothy Granade, Chou-Pong Pau, Susan Wells, Sherry Owen
CDC Reference Number: I-033-08

Detection of HIV-1 p24 Antigen and HIV Specific Antibodies Using a Rapid, Paramagnetic Lateral Flow Assay

This invention provides a quick, inexpensive and technically facile method, in the form of a testing strip to detect HIV. This rapid, paramagnetic lateral flow assay detects HIV-specific antibodies and the HIV-1 p24 antigen using magnetic platform technology. This test complements detection assays that are currently being developed using this same technology for other infectious agents. Because the assay is quantitative, the test is potentially more sensitive than other rapid tests currently in use.

Inventors: Timothy Granade, Chou-Pong Pau, Susan Wells, Shon Workman
CDC Reference Number: I-018-08

Utilization of loop-mediated isothermal amplification (LAMP) for the Detection of HIV-1 Infection

This invention describes the use of a cost effective, one-step rapid nucleic acid test for diagnosing HIV-1 infection. It involves the use of the loop-mediated isothermal amplification method for amplifying DNA and RNA (LAMP and RT-LAMP, respectively). Detection of HIV DNA can occur as early as 2 weeks after infection, allowing for detection of the virus during the highly infectious 4-5 week period post-infection and pre-seroconversion. This process utilizes four HIV-1 specific primers. Because this method is rapid and requires minimal equipment, it can be used at point-of-care and resource-poor environments.

Inventors: Sherry M. Owen, Curtis Kelly, Donna Rudolph
CDC Reference Number: I-021-07

Soluable Human Dendritic Cell Specific ICAM-3 Grabbing Non-Integrin (shDC-SIGN)

The contribution of dendritic cells to mucosal HIV transmission may be largely mediated by the surface expression of dendritic cell specific-ICAM-3 grabbing non-integrin (DC-SIGN). This glycoprotein, a C-type lectin, binds to the envelope protein of HIV, gp120. Soluble human DC-SIGN (shDC-GIGN) blocks HIV-1 binding to cell surface DC-SIGN. Thus, shDC-SIGN will be a useful agent for evaluating the contribution of DC-SIGN in mucosal HIV transmission and may ultimately give rise to a novel class of inhibitors.

Inventors: Butera Salvatore, Jia Hongwei
CDC Reference Number: I-012-03

A Simple Assay for Detecting Recent HIV-1 Infection and Estimating Incidence

This invention is a simple enzyme immunoassay that detects increasing levels of anit-HIV-IgG after seroconversion and can be used for detection recent HIV-1 infection. The assay, termed IgG-Capture BED-EIA, incorporates a branched peptide derived from 3 different subtypes to allow equivalent detection of antibodies of different subtypes. The competitive format of the assay allows detection of increasing proportion of HIV-1 IgG for almost 2 years after seroconversion.

Inventors: Steve McDougal, Bharat Parekh
CDC Reference Number: I-021-02

Development of a Chimeric Recombinant HIV-1 Envelope Protein Derived from Immunodominant Region (IDR) of Multiple Subtypes

This invention comprises a recombinant HIV protein (rIDR-M) expressed in *E. coli*. The recombinant protein incorporates 3 sequences derived from immunodominant region of gp41, representing divergent HIV-1 subtypes A through E (group M). The protein has a Histidine tag at the N-terminus which helps in purification of the protein. In addition, 3 sequences are separated by hydrophilic spacer sequences to increase yield and solubility of the purified recombinant protein. It has been shown to detect HIV antibodies to divergent HIV-1 viruses with high sensitivity. This technology also details a process that has been developed to produce significant quantities of purified rIDR-M from *E. Coli*, providing a continuous source of consistent product.

Inventors: Bharat Parekh, Xierong Wei, Steve McDougal
CDC Reference Number: I-002-04

Method and Kit for Detecting Resistance to Antiviral Drugs

One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention provides for an assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drug in a biological sample.

Inventors: Shinji Yamamoto, Gerardo Lerma, William Switzer, Walid Heneine, Thomas Folks
CDC Reference Number: I-005-98
Patent Number: 6,787,126

Method and Kit for Detecting Resistance to Antiviral Drugs

One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention adds multi-drug resistance testing to the assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drugs described in I-005-98.

Inventors: Walid Heneine, Shinji Yamamoto, Gerardo Lerma, William Switzer, Thomas Folks
CDC Reference Number: I-004-02

Methods and Compositions for Inhibition of Viral Replication

This invention relates to the identification of a cellular enzyme (casein kinase II) which, when inactivated by chemical inhibitors, results in the inability of the cell to support the replication of HIV-1. This discovery is unique because the drug target is cellular rather than viral, which may greatly reduce the ability of the virus to develop resistance to the drug. Since there are no anti-HIV-1 drugs currently available which have this property, the present invention fills the need to develop novel HIV-inhibitory agents for possible therapeutic use.

Inventors: Jennifer Brown, Thomas Folks, Walid Heneine, Paul Sandstrom, William Switzer
CDC Reference Number: I-012-96
Patent Number: 6,274,611

Methods and Reagents for Molecular Detection of HIV-1 Groups

This invention provides reagents and assays for detecting HIV-1 groups M and O and optionally HIV-1 group N and SIVcpz. Nucleic acid primers for the hybridization to, amplification, and subsequent detection are also provided for. The nucleic acid amplification assays can detect small concentrations of HIV and are also useful for qualitative and quantitative examinations.

Inventors: Danuta Pieniazek, Chunfu Yang, Renu Lal
CDC Reference Number: I-020-98
Publication Number: WO0046403

Development of a HIV-1 Multi-Clade, Multivalent (HIV1MCMV) Recombinant Vaccine Construct

Most HIV-1 vaccine constructs are subtype-specific and designed to prime only one arm of the immune system. Thus, they are not expected to protect against diverse natural HIV-1 infections. Data from vaccine trials suggest that additional epitopes as well as activation of both arms of the immune system may be required for an effective HIV-1 vaccine. As the HIV epidemic continues to spread world wide, the need for an effective vaccine remains urgent. This invention addresses this need through a multi-epitope, multi-clade HIV1 vaccine construct that will provide a universal vaccine for all parts of the world affected by the epidemic. The design of the construct allows for the addition or deletion of epitopes and contains specific cellular targeting epitopes that should permit optimization for better antigen processing and recognition. The construct might be combined with other epitope based constructs to develop multi-pathogen vaccines.

Inventors: Renu Lal, Sherry Owen
CDC Reference Number: I-013-03
Patent Number: 7,425,611

Development of a Rapid HIV Diagnostic Assay for Diagnosis and Detection of Recent and Long Term HIV-1 Infection

This technology provides the necessary information for the development of a device for simultaneous rapid diagnosis of HIV infection and for identification of recent HIV-1 infection. The device will utilize immunochromatographic or flow-through principles to detect HIV antibodies. The device will have two areas, one for diagnosis of HIV infection and a second to distinguish recent infection (<6 months) from long-term infection. The addition of this second area can have added significance for surveillance, counseling, partner notification and other prevention activities, including the estimation of HIV incidence in cross-sectional populations. The proposed device would utilize a single platform that contains all of the required reagents, making it simple and easy to use. The entire testing process, including the determination of incident infections, will be done in less than 20 minutes. The detection of recent infection is important for incidence measurements and for targeting prevention activities and resources. Incidence also serves as an indicator of the effectiveness of intervention strategies. The demand for incidence is increasing worldwide as the global effort to reduce the spread of AIDS expands.

Inventors: Timothy Granade, Bharat Parekh, Chou-Pong Pau
CDC Reference Number: I-003-04

Development and Characterization of Large Volume Panels of Plasma, PMBC, and DBS from HIV Strains from West Africa

There is expanding interest in using new and existing diagnostic and clinical assays for detecting and monitoring HIV infections in Africa. Currently, large volume panels of serologically and genetically characterized HIV-1 subtypes and recombinant strains from West and Central Africa do not exist for evaluating the type of diversity found in these regions. CDC has obtained a large number of discarded blood bank samples from these regions. Characterization of these samples provide a unique and valuable set of reagents for vaccine trials, quality assurance, quality control, proficiency panels, and evaluation of new and existing serologic and genetic assays for use in Africa..

Inventors: Marcia Kalish, Salvatore Butera, Thomas Folks, Danuta Pieniazek, Amanda Schaefer, Ae Saekhou Youngpairoj, John Nkengasong
CDC Reference Number: I-006-04

Multiple Antigenic Peptide Assay for Detection of HIV or SIV Type Retroviruses

Human immunodeficiency virus (HIV) is subdivided into 2 types, HIV-1 and HIV-2, both of which are believed to be the result of zoonotic transmission. Humans are being increasingly exposed to many different simian immunodeficiency viruses (SIVs) in wild primates, for example through the hunting and butchering trade in Africa. This human exposure to SIVs may lead, or has already led, to transmission of SIVs with the potential to cause new epidemics. Unfortunately, new zoonotic transmissions may go undetected because of the lack of SIV-specific tests. Thus, there is the potential to compromise the safety of the blood donor supply system and possibly to seed a new HIV-like epidemic. This invention addresses these problems by providing a way to test for the many divergent strains in monkeys and humans to identify primary infection and prevent secondary transmission.

Inventors: Marcia Kalish, Tom Folks, William Switzer, Chou-Pong Pau, Clement Ngondmo
CDC Reference Number: I-023-02
Publication Number: WO/2004/092724

RAB9 and Uses Thereof Related to Infectious Disease

This invention comprises methods for reducing the activity of Rab9A or Rab11A, by reducing the activity of a modulator thereof that increases Rab9A or Rab11A activity, to treat or reduce infection or other stage of the life cycle of a pathogen, such as a virus. The technology also addresses methods of identifying agents involved in pathogen infection, such as modulators of Rab9A and Rab11A.

Inventors: Thomas Hodge, Natalie McDonald, Donald Rubin, Michael Shaw, Anthony Sanchez, James Murray
CDC Reference Number: I-036-04
Publication Number: WO/2005/092924

Simple, Rapid, and Sensitive Real-Time PCR Methods for Detecting Drug Resistance in Human Immunodeficiency Viruses (HIV)

Mutations that confer resistance to antiretroviral drugs are expected to increase as use of these drugs for the clinical management of HIV-1 infected people increases worldwide. Resistance-related mutations are conventionally detected by sequence analysis of viral RNA from plasma. The sensitivity limitations of conventional sequence analysis make it difficult to measure low levels of mutants, such as what might be present early in the emergence of resistance or which might persist at low set points in the absence of treatment. Real-time PCR assays can provide a more user-friendly, less expensive, and more sensitive method for detecting drug resistance-associated mutations, and thus, can be a powerful screening tool for surveillance and as a cost effective screen for treatment-related resistance. This invention allows real-time PCR-based testing for different point mutations in patient samples at an achievable sensitivity of 1-2 log greater than conventional sequencing. The assay measures the differential amplifications of common and mutation-specific reactions that target codons of interest. Given the low cost, high-throughput capability, and greater sensitivity than conventional testing, these assays will be useful for detecting drug resistance-associated mutations and could aid in the clinical management of HIV-1 infection.

Inventors: Jeffrey Johnson, Walid Heneine
CDC Reference Number: I-005-03
Publication Number: WO/2005/121379

Recombinant Infectious Clone of Simian Foamy Virus (SFV) Expressing HIV-1 gp 120 for Vaccine Purposes

This invention uses a reengineered Simian Foamy Virus (SFV) to deliver long term immunization against HIV to patients. An HIV-1 gene is inserted into an infectious molecular clone of SFV and injected into the patient, thus causing the host's own cells to produce the gp120 glycoprotein for the life of the infected cells. As a result, the recombinant SFV clone constantly stimulates the immune system and sustains the antibody response to HIV, thereby obviating the need for booster immunizations. SFV has distinct advantages over other delivery methods because it causes no harm to the host and is rarely seen in the human population.

Inventors: Thomas Folks, James Smith
CDC Reference Number: I-004-06

Prevention of Rectal HIV Transmission

This invention discloses the use of a Tenofovir/FTC combination to prevent rectal HIV transmission. Available data shows that Tenofovir alone is not sufficient to protect against SHIV mucosal infection. This invention shows chemoprophylaxis in combination with retrovirals provides a high level of protection against not only initial viral exposure, but also repeated virus challenges.

Inventors: Walid Heneine, Thomas Folks, J. Gerardo Garcia-Lerma, Ronald Otten
CDC Reference Number: I-022-06
Publication Number: 20070265227

A Novel Simian T-cell Lymphotopic Virus, Designated STLV-5

Human T-cell lymphotopic viruses types 1 and 2 (HTLV-1 and HTLV-2) have spread globally and cause diseases such leukemia, lymphoma, and neuralgic disorders. Both HTLV-1 and HTLV-2 are believed to have originated from cross-species transmission of simian T-cell lymphotrophic viruses (STLV) from infected nonhuman primates. Cross-species transmission of STLV-like viruses to humans in West and Central Africa have led to the discovery of the novel viruses HTLV-3 and HTLV-4. The current discovery involves STLV-5, a novel virus discovered from a monkey *(Cercopithecus mona)* in Cameroon. The discovery of STLV-5 may indicate that a similar virus (HTLV-5) may be spreading undetected in humans.

Inventors: William M. Switzer, Walid M. Heneine, Thomas M. Folks, Nathan D. Wolfe, Donald S. Burke
CDC Reference Number: I-033-06

Novel Human T-Cell Lymphotropic Virus, Designated HTLV-3

The human T-Cell lymphotropic virus (HTLV) is known to cause leukemia, lymphomas, and neurological diseases and is part of routine blood screening. The present invention discloses novel HTLV viruses which are distinct from HTLV1 and HTLV-2 and more closely related to simian T-cell lymphotrophic viruses, type 3 and 4. The viruses, tentatively called HTLV-3 and HTLV-4 may be endemic among humans and are likely the human counterparts to STLV-3 and STVL-4. Like HTLV-1 and HTLV-2, these viruses may be the causative agents of human diseases.

Inventors: William Switzer, Walid Heneine, Thomas Folks, Nathan Wolfe, Donald Burke, Eitel Mpoudi-Ngole
CDC Reference Number: I-019-04
Publication Number: WO/2006/091511

Methods for Sensitive Detection of Reverse Transcriptase

Retroviruses are widely distributed in vertebrates and are known to cause a variety of diseases in man and animals including immunodeficiencies, leukemias and lymphomas. The entire retrovirus family is characterized by the presence of a unique enzyme, reverse transcriptase (RT), which transcribes the viral genomic RNA into a double-stranded DNA copy. This invention provides a method for detecting a retrovirus in a biological sample by identifying the presence of RT, and further allows for differentiating between infection by HIV-1 Group M and Group O in a HIV-1 infected subject.

Inventors: Thomas Folks, Walid Heneine, William Switzer, Shinji Yamamoto
CDC Reference Number: E-232-93
Patent Number: 5,849,494

Methods for Sensitive Detection of Reverse Transcriptase

Retroviruses are widely distributed in vertebrates and are known to cause a variety of diseases in man and animals including immunodeficiencies, leukemia's and lymphomas. The entire retrovirus family is characterized by the presence of a unique enzyme, reverse transcriptase (RT), which transcribes the viral genomic RNA into a double-stranded DNA copy. This invention provides a method for detecting a retrovirus in a biological sample by identifying the presence of RT.

Inventors: Shinji Yamamoto, Walid Heneine, William Switzer, Thomas Folks
CDC Reference Number: E-232-93
Patent Number: 6,136,534

Method and Kit for Detecting Resistance to Antiviral Drugs

One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention provides for an assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drug in a biological sample.

Inventors: Shinji Yamamoto, Gerardo Lerma, William Switzer, Walid Heneine, Thomas Folks
CDC Reference Number: I-005-98
Publication Number: 6,787,126

Compositions, Methods and Devices for Detection of Retroviral Infection

Currently, there are shortages of organs, tissues and cells for transplantation into humans. These shortages, combined with recent advances in transplantation immunology, have provided impetus for the development of xenotransplantation - the therapeutic use of living animal tissues and organs in humans. Pigs are among the primary species proposed as sources of xenografts. In response to recent concerns regarding the transmission of infectious agents from animals to humans, a method was developed to detect porcine retroviral agents. This method detects the presence of human antibodies created in response to exposure to such agents in a xenotransplant recipient.

Inventors: Walid Heneine, William Switzer, Thomas Folks, Paul Sandstrom, Aprille Matthews
CDC Reference Number: I-021-98
Patent Number: 6,596,478

Methods and Devices for Detection of Xenogenic Graft Persistence

Currently, there are shortages of organs, tissues and cells for transplantation into humans. These shortages, combined with recent advances in transplantation immunology, have provided impetus for the development of xenotransplantation - the therapeutic use of living animal tissues and organs in humans. Pigs are among the primary species proposed as sources of xenografts. In response to recent concerns regarding the transmission of infectious agents from animals to humans, a method was developed to detect porcine endogenous retroviral (PERV) agents. The compositions, methods and devices are useful for determining or monitoring graft survival and rejection in recipients of xenografts and are useful for detecting PERV infections in a xenotransplant recipient or donor. In addition, the compositions, methods and devices are useful for screening therapeutic products to be administered to humans to ensure that the products are free of PERV contamination prior to administration.

Inventors: William Switzer, Shanmugam Vedapuri, Walid Heneine
CDC Reference Number: I-024-98
Patent Number: 6,566,102

Human Papillomavirus

Human Papillomavirus (HPV) Variant Assignment by Pyrosequencing

Human Papillomavirus (HPV) has been associated with an increased risk of cervical disease. Currently available tests only detect HPV in samples containing one variant and use conventional and slow viral genome DNA sequencing. This invention uses pyrosequencing to allow for rapid sequencing and detection of multiple HPV variants.

Inventors: David Swan, Kara L. Duncan, Mangalathu S. Rajeevan, Elizabeth R. Unger, Josef Limor
CDC Reference Number: I-028-05

Influenza

Real-Time TaqMan RT-PCR for Human Parainfluenza Virus 4

Human parainfluenza virus 4 is an important agent of pediatric respiratory tract disease. This invention includes real-time RT-PCR assays that were developed for detection of parainfluenza virus 4 as well as for distinguishing between the parainfluenza virus and influenza. The unique primer and probes set allow for the direct detection of the human parainfluenza virus 4 respiratory viral pathogen in human clinical samples.

Inventors: Dean Erdman, Ryan Dare
CDC Reference Number: I-020-10

Improved Methods for Data Analysis of Influenza Microneutralization

The Microneutralization assay measures the ability of serum samples to neutralize the influenza virus. The invention is a set of SAS based programs that apply improved methods of data analysis to the Influenza Microneutralization assay. The program uses 4-parameter logistic curve fitting algorithms to interpolate between the individual data points, allowing improved accuracy and precision for neutralization titers. This method allows every experiment to be analyzed the same way, provides greater accuracy by interpolating curve fits between dilutions, prevents transcription errors or manual calculation errors, develops and applies consistent and quantitative quality control rules, and operates at a more efficient speed.

Inventors: Jarad Schiffer, Dr. Kathy Hancock
CDC Reference Number: I-005-10

Simultaneous Detection and Quantification of Influenza Proteins in Complex Matrices

This invention is a method for identifying and quantifying a group of influenza proteins. Specifically, conserved peptides from the proteins of influenza (hemagglutinin, neuramidase, matrix 1 and 2, and nucleoprotein) have been synthesized and labeled to be used as internal standards for the quantification of those proteins in a complex (biological or manufactured) matrix. One or more of these peptides can be used to simultaneously detect and quantify the target proteins in one analysis using multiple reaction monitoring (MRM) isotope mass spectrometry (IDMS). This method for quantifying influenza proteins and peptides in samples has potential for improving the quality control and, therefore, the profitability of influenza vaccines.

Inventors: John R. Barr, Zhu Guo, Ruben O. Donis, Tracie L. Williams, Leah G. Luna, Jim Prikle
CDC Reference Number: I-024-07
Publication Number: WO/2009/110873

Mouse Monoclonal Antibodies Specific for the H5 Hemagglutinin of Avian Influenza Virus

Avian influenza virus can be carried worldwide by wild birds, and can spread to other animals and humans. Avian influenza viruses may result in normal flu symptoms, eye infections, pneumonia, severe respiratory diseases, and other severe and life-threatening complications. Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population. This invention concerns mouse monoclonal antibodies to the H5 hemagglutinin of a highly pathogenic avian influenza virus subtype. These antibodies can be used for diagnosis of avian flu in animals and humans, for monitoring and standardizing vaccine production to control, prevent, detect, and/or treat infections in people, or for further studying the avian influenza virus in the lab.

Inventors: Donis O. Ruben, Judith A. Appleton, Lucille F. Gagliardo
CDC Reference Number: I-007-07

Enhancing Disease Resistance against RNA Viral Infections

This invention proposes a novel way of improving our body's ability to resist infectious diseases caused by RNA viruses, such as influenza, Respiratory Syncytial Virus, as therapeutic to cure RNA viral infections, and boosting immune responses against preventive vaccines. The physical and functional integrity of an individual against disease caused by a variety of microorganisms is maintained in part by the dynamic barrier provided by the skin and the epithelial linings of the gastrointestinal, respiratory and urogenital system. These prevent entry and colonization of potential pathogens. Epithelial cells that comprise the barrier wall express pathogen sensors, pattern recognition receptors (PRRs), such as toil-like receptors (TLRs) capable of responding to pathogen associated molecular patterns (PAMPs). Upon PAMP recognition, these cells secrete several types antibacterial peptides, namely defensins, cathelicidins and dermicidins. When the epithelial integrity is breached and the pathogens gain access to our tissues and cells. Once pathogens gain access into cells, pathogen sensors such as TLR3, 7, 8, and 9 which are located in the endocytic vesicles recognize the pathogens and generate innate immune responses to remove pathogen from the system. However, the pathogens have developed strategies to overcome these defenses and escape into cytosol of the infected cell. However, there are a number ofintracytoplasmic pathogen sensors such as Nodl/2, IPAF, Nalps, and MDA5 and RIG-I recognize the pathogens and initiate innate immune response to eliminate them. The present invention will enable us to confer disease resistance against the RNA viral infections, treat individuals infected with RNA viruses, and enhance the immunogenicity and efficacy of both preventive and therapeutic vaccines. This invention can be extended to other bacterial, viral, parasitic, and fungal diseases with the other pathogen sensors.

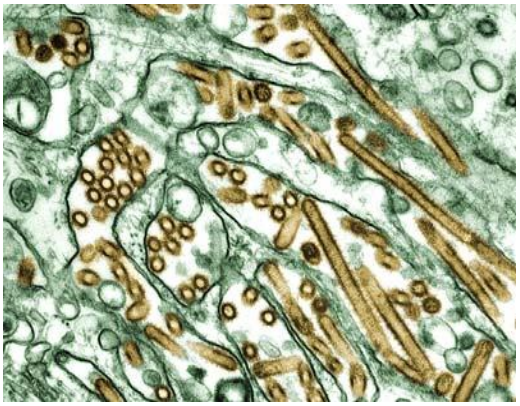
Inventors: Suryaprakash Sambhara, Zhu Guo
CDC Reference Number: I-051-06
Publication Number: WO/2008/048976

Preparation and Use of Recombinant Influenza A Virus M2 Constructs and Vaccines

M2, a structurally conserved influenza A viral surface protein, is capable of inducing broader, more cross-reactive immunity to type A influenza viruses. This invention solves the problems of the prior art approaches to recombinant M2 production by providing new recombinant forms of M2 whose structure has been modified to allow simple prokaryotic expression as a soluble, readily purified variant protein which retains antigenic and immunogenic properties. The invention relates to vaccines comprised of these new recombinant forms of M2, and to methods of prevention and treatment of influenza A virus infections.

Inventors: Jacqueline Katz, Alan Frace, Alexander Klimov
CDC Reference Number: I-020-97
Patent Number: 6,169,175

Primer and Probes for Detection and Discrimination of Types and Subtypes of Influenza Viruses by Real-Time RT-PCR



This method allows for a rapid detection and identification of types and subtypes of influenza viruses. This includes avian influenza subtypes that have been shown to infect humans and may have pandemic potential. This protocol includes the only available primer/probe sets to specifically and sensitively detect highly pathogenic H5N1 viruses circulating currently in South East Asia.

Inventors: Stephen Lindstrom, Alexander Klimov, Nancy Cox, Lamorris Loftin
CDC Reference Number: I-007-05
Publication Number: WO/2007/095155

Measles

Measles Virus Specific Antibody Detection Using Recombinant Measles Proteins

Current technology for measles virus detection relies on the use of whole virus and antigen in an enzyme immunoassay format. Generation of a recombinant nucleoprotein in the baculovirus expression vector system eliminates the use of whole virus and supplies an abundant source of antigen necessary for the evaluation of seroconversion and seroprevalence rates within vaccinated populations. Additionally, use of this recombinant antigen provides greater reproducibility with decreased cross-reactivity to human serum proteins.

Inventors: Kimberly Hummel, Dean Erdman, William Bellini, Janet Heath
CDC Reference Number: E-043-92
Publication Number: WO9322683

Norovirus

A Monoclonal Antibody (McAb-NoV) Which is Cross-Reactive to at Least 2 Genogroup I Strains and 8 Genogroup II Strains of Noravirus in the Family Caliciviridae

Noroviruses are the most common cause of outbreaks of viral gastroenteritis (stomach pain, diarrhea, and vomiting) and the second most common illness in the United States after the common cold. Of the five genogroups of norovirus, genogroup I and II are the most important human pathogens. This invention concerns a monoclonal antibody that is broadly reactive against several known norovirus strains. It is cross-reactive to at least 2 (of 8) genogroup I strains, and 8 (of 19) genogroup II strains. This antibody has the potential to form the foundation of an immuno-based assay for the detection of norovirus infection in patient samples, and when coupled with type-specific antibodies, has the potential not only to allow the detection of norovirus antigen, but also allow the typing of the infecting strain.

Inventors: Jan Vinje, Steve Monroe, John C. Hart, Jr.
CDC Reference Number: I-020-07

Orthopoxvirus

Rapid Protein-Based Diagnostic Test System that Can Detect Exposure to or Presence of Orthopoxviruses

Technology constraints such as a lack of refrigeration and electricity frequently provide barriers to efficient disease detection and bioterrorism surveillance. This CDC assay uses virus protein and virus antibody for rapid detection of exposure to orthopoxviruses. Orthopox detection can be performed in less than two minutes and in remote areas with no access to traditional laboratory equipment.

Inventors: Kevin L. Karem, Zachary Braden
CDC Reference Number: I-028-06

Monoclonal Antibodies Specific for Variola Virus

This technology comprises two series of monoclonal antibodies which specifically recognize the variola virus which causes smallpox. The first monoclonal recognizes variola but not other closely related orthopox viruses in ELISA assays, while the second monoclonal recognizes variola as well as camelpox and other related orthopox viruses. The antibodies can be used to create novel tests for variola virus using both clinical and environmental samples. They also may be used to study the biology of the variola virus during infection and create therapeutic treatments.

Inventors: Inger Damon, Scott Smith, Joanne Patton, Kevin Karem, Dennis Bagarozzi, John Hart, John Kools, Gin Lou
CDC Reference Number:I-009-06

Diagnostic Assay for Orthopoxviruses Other than Variola

A new real-time PCR based diagnostic assay was designed that targets the DNA polymerase gene of all Eurasian orthopoxviruses other than variola (smallpox). This gene target is highly conserved and required for a productive viral life cycle, ensuring all infectious orthopoxviruses will retain this gene. The assay assists in the diagnosis of orthopoxviral infections (ex. vaccinia, cowpox, monkeypox) which affect humans. Since the assay does not detect variola, a rash illness can be confirmed as an orthopoxviral infection that is not smallpox at the same time. The assay is also much more sensitive than available standard PCR tests.

Inventors: Yu Li, Inger Damon, Victoria Olson
CDC Reference Number: I-026-04

Diagnostic Assay for Cowpox

This real-time PCR based assay accurately detects trace amounts of cowpox. Unlike currently available tests, this real-time PCR assay uniquely identifies cowpox among all possible orthopox viruses using a small region of DNA found uniquely in the cowpox species of orthopox viruses. This assay can successfully identify cowpox when the clinical sample contains as few as 150 viral copies. As a result, this test is much faster and more sensitive than currently available PCR tests.

Inventors: Yu Li, Inger Damon
CDC Reference Number: I-034-05

Therapeutic Treatment of Poxvirus Infections

This invention covers an antiviral-like therapeutic treatment for poxvirus, the cause of monkeypox, molluscum contagiosm, smallpox, and other diseases. In *in vitro* experiments, this compound substantially reduced the amount of plaques formed. As a result, this drug may be developed for therapeutic treatment of Poxvirus infections. Such treatments could be especially important in the event of a smallpox outbreak, as vaccinations against the virus have not been widely administered for the last thirty years.

Inventors: Kemba Lee, Russell Regnery
CDC Reference Number: I-019-06

Parechovirus

Three Parechovirus Diagnostic Assays Utilizing Real Time Taqman or Seminested RT-PCR

Similar to the enteroviruses, parechoviruses are responsible for gastrointestinal, respiratory and central nervous system infections. The CDC developed a real time reverse transcription-polymerase chain reaction (RT-PCR) Taqman assay and an RT-semi-nested PCR (RT-snPCR) assay for the detection of parechoviruses. All tests target conserved regions in the 5' nontranslated region (5'NTR) of the parechovirus genome and share forward and reverse primers. The Taqman probe and RT-snPCR nested primer target the same conserved site but vary in length. All three assays detect all known human parechoviruses (PPeV) and Ljungan viruses (LV), unlike other published parechovirus 5' NTR assays, which only detect a limited number of PPeV types. All these assays are more sensitive than cell culture and all may be used to test isolates or original clinical specimens.

Inventors: William A. Nix, M. Steven Oberste
CDC Reference Number: I-023-05
Publication Number: WO/2007/133189

Poliovirus

Group, Serotype, and Vaccine Strain-Specific Identification of Polioviruses by Real-Time PCR

While the current diagnostic RT-PCR kits are highly accurate and reliable in identifying poliovirus, this method is especially laborious for laboratories with large workloads. Furthermore the high variability and rapid evolution of the poliovirus RNA genome created a need for this new method. The invention is an adaptation of a previously described poliovirus diagnostic reverse transcriptase-PCR (RT-PCR) assay to a real-time RT-PCR (rRT-PCR) format. The development of the real-time RT-PCR has opened the way for more-rapid and more-accurate diagnostic arrays. This technology allows for the rapid and large-scale identification of poliovirus field isolates.

Inventors: David Kilpatrick, Chun-Fu Yang, Raymond Campagnoli, Lina De, William Nix, Olen Kew, Karen Ching, Jane Iber, Annelet Vincent, Su Yang, Mark Mandelbaum
CDC Reference Number: I-017-09

Modulation of Poliovirus Replicative Fitness by Deoptimization of Synonymous Codons

Infections by intracellular pathogens such as viruses, bacteria and parasites, are cleared in most cases after activation of specific T-cell immune responses that recognize foreign antigens and eliminate infected cells. Vaccines against those infectious organisms have been traditionally developed by administration of whole live attenuated or inactivated microorganisms. Although research has been performed using subunit vaccines, the levels of cellular immunity induced are usually low and not capable of eliciting complete protection against diseases caused by intracellular microbes. However, CDC inventors discovered that replacement of one or more natural (or native) codons in a pathogen with synonymous unpreferred codons can decrease the replicative fitness of the pathogen, thereby attenuating the pathogen. The unpreferred synonymous codon(s) encode the same amino acid as the native codon(s), but have nonetheless been found to reduce a pathogen's replicative fitness. This invention teaches compositions and methods that can be used to develop attenuated vaccines having well-defined levels of replicative fitness and enhanced genetic stabilities.

Inventors: Olen Kew, Cara Burns, Jing Shaw, Raymond Campagnoli, Jacqueline Quay
CDC Reference Number: I-025-04
Publication Number: WO/2006/042156

Rabies

Pan-Lyssavirus Vaccines Against Rabies

Lyssaviruses are single-stranded RNA viruses which cause rabies and rabies-like diseases in mammals. Based on phylogeny, immunogenicity, and virulence of lyssavirus isolates, two lyssavirus phylogroups have been proposed. Currently available commercial vaccines are considered to be effective against infections from phylogroup I, however, these vaccines do not offer full protection against infection from viruses outside of phylogroup I. Recombinant rabies viruses have been developed which have glycoprotein genes from at least two different lyssaviruses. These can be used as pan-lyssavirus vaccines to provide protection against infection by multiple genotypes of lyssavirus. Further, a vector comprising full-length rabies virus antigenomic DNA is provided, as well as cells comprising a rabies virus vector. Finally, methods have been developed which offer a means of eliciting an immune response in a subject against lyssavirus by administering to the subject one or more of the recombinant rabies viruses.

Inventors: Xianfu Wu, Charles Rupprecht, Ivan Kuzmin

CDC Reference Number: I-002-10

A New Lyssavirus: Shimoni Bat Virus (SHIBV)

The *Lyssavirus* genus contains the more commonly known rabies virus that kills between 50,000 and 60,000 humans annually. A novel strain in the rabies family of viruses, the Shimoni bat virus, has been discovered, with phylogenic and antigenic patterns which identified it as a new species of *Lyssavirus*. Phylogenic reconstructions of the Shimoni bat virus and monoclonal antibody typing were used to demonstrate a distinct genetic antigenic pattern. This unique genetic information may be used to create antigens or vaccines against the Shimoni bat virus, and provides opportunity for the development of new diagnostics, therapeutics, and prophylactic therapies for viral infection.

Inventors: Ivan Kuzmin, Anne Mayer, Michael Niezgoda, Bernard Agwanda, wanda Markotter, Robert Breiman, Charles Rupprecht

CDC Reference Number: I-033-09

Simplified Method for Whole Genome Sequencing of Lyssaviruses

This technology can be used for rabies tracking as well as potentially used to develop a rabies vaccine (and it may be useful for other viruses as well). In many countries, rabies surveillance is lacking. The majority of lyssavirus isolates are not identified, and the actual significance of LBV and other lyssaviruses for public health is unknown. All despite the fact that rabies kills 40,000 to 70,000 people per year. This technology concerns a method that can be used for sequencing the entire lyssavirus genome from field samples. This circularization method has never been applied to lyssaviruses, but had been developed for several other viruses and in each case, involved the use of genomic RNA, purified from high-passage material. Multiple passages in laboratory models may cause mutations, compared to the original field material. Therefore, our method is not only significantly simplified but also gives potentially more accurate output.

Inventors: Ivan Kuzmin, Xianfu Wu
CDC Reference Number: I-018-07

Vector for Recombinant Poxvirus Expressing Rabies Virus Glycoprotein

Rabies vaccines presently in use generally contain preparations of inactivated or attenuated live rabies virus. Such preparations might be relatively costly, biologically unstable, or produce vaccinal side effects. Hence, the need remains to provide for humans and animals an efficacious vaccine against rabies that would be potent, less perishable, less costly, and having diminished or no vaccinal side effects compared to present rabies vaccines. A vaccinia virus recombinant construct has been developed that expresses the gene for rabies virus glycoprotein. Recombinants may used for vaccines and could also be readily adapted for production of related antigen, antibody, and other immunobiological reagents

Inventors: Joseph Esposito, Kathleen Brechling, Bernard Moss
CDC Reference Number: E-359-86
Patent Number: 5,348,741

Method of Sequencing Rabies Whole Genome and its Application in Vaccine Development

The critical feature of this technology is the ERA rabies whole genome DNA sequence. With the availability of the entire rabies genome, a recombinant vaccine can be developed using reverse genetics. The vaccines that can be developed using this genome are fundamentally different from classic ones that are being produced. The technology is also being applied to other negative stranded RNA viruses.

Inventors: Xianfu Wu, Charles Rupprecht
CDC Reference Number: I-027-04
Publication Number: WO/2007/047459

Respiratory Syncytial Virus

RSV Vaccine: Use of the Central Conserved 13 Amino Acids or Conserved Group-Specific Amino Acid Sequence of the G Protein

Respiratory Syncytial Virus (RSV) is the most common cause of serious respiratory disease in infants and young children and an important cause of disease in the elderly. Efforts to make a safe and effective vaccine to date have failed. A formalin inactivated vaccine given to young children in some cases led to more serious diseases with later RSV infection leading to concerns whether non-live RSV vaccine may be unsafe in young children. Further, this vaccine was incapable of inducing a highly effective protective immune response. This invention is designed to address both problems. A vaccine based on amino acid sequences that correspond to group specific regions of the G protein can effectively induce antibodies, facilitate virus clearance, decrease the virus induced inflammatory response to RSV challenge and decrease the enhanced disease with RSV challenge. This composition may be used alone as a vaccine to safely protect infants, children, and adults from RSV, or as a booster with other RSV proteins or with inactivated virus as a vaccine to ensure that it can be given safely and effectively improve protection from RSV.

Inventors: Larry Anderson, Lia Haynes, Ralph Tripp
CDC Reference Number: I-021-09
Patent number: WO/2011/017442

Real-Time TaqMan® RT-PCR for Human Metapneumovirus, Human Parainfluenza Virus 1; 2; and 3, and Human Respiratory Syncytial Virus

These CDC assays describe a real-time reverse polymerase chain reaction (PCR) assay using TaqMan® chemistry for detection of human metapneumovirus (HMPV), human parainfluenza virus 1 (HPIV1); 2 (HPIV2); and 3 (HPIV3), and the human syncytial virus (HRSV) in genomic RNA in clinical specimens. Unique oligonucleotide primer and probes are designed to target regions of various protein genes of each virus. These assays can be used to diagnose acute respiratory illness and can facilitate surveillance testing for pandemic influenza.

Inventors: Dean D. Erdman, Ryan K. Dare
Metapneumovirus, CDC Reference Number: I-036-06
Parainfluenza Virus 1, CDC Reference Number: I-037-06
Parainfluenza Virus 2, CDC Reference Number: I-038-06
Parainfluenza Virus 3, CDC Reference Number: I-039-06
Respiratory Syncytial Virus, CDC Reference Number: I-040-06

Compositions and Methods for Modulating RSV Infection and Immunity

RSV is the single most important cause of lower respiratory tract disease in children. Many vaccination strategies have been attempted, but as of yet none have been successful. This invention relates to the discovery of functional motifs in the RSV G protein that may provide new insights into the past vaccine failures and may lead to immunogenic modifications that would provide a safe and efficient RSV vaccine.

Inventors: Ralph A Tripp, Les Jones, Larry J Anderson
CDC Reference Number: I-022-00
Publication Number: 20040009177

CD40 Ligand Adjuvant for Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) has long been recognized as a major viral pathogen of the lower respiratory tract of infants. Successful methods of treating or preventing RSV are currently unavailable. CD40 ligand (CD40L) is an important costimulatory molecule on the T-cell and is central to the development of immunity. CD40L can be used as an adjuvant to enhance cytokine and antibody response to RSV.

Inventors: Ralph Tripp, Michael Brown
CDC Reference Number: I-029-99
Patent Number: 7,371,392

Macroaggregated Albumin-Polyethylenimine (MAA-PEI) Lung-Targeted Delivery of RSV DNA Vaccines

Currently, no safe and effective RSV vaccine is available. DNA vaccines encoding RSV F or G glycoproteins are one RSV vaccine option being examined for safety and efficacy. However, DNA vaccination has been problematic because of the need for repeated vaccination requiring large amounts of DNA, and DNA vaccination does not often result in mucosal immunity. Macroaggregated albumin (MAA) has been used for many years in imaging pulmonary blood flow, as the size of MAA results in these particles being trapped in the lung arterioles. This invention demonstrates that MAA conjugated to polyethylenimine (MP) is a useful carrier to deliver RSV-DNA vaccines to the site of RSV infection (lungs) and may be effective at enhancing RSV immunity.

Inventors: Ralph Tripp, Jennifer L. Harcourt
CDC Reference Number: I-026-01
Publication Number: 20040009903

Rhinovirus

Real-time TaqMan RT-PCR Assays for Human Rhinovirus

This technology is a real-time TaqMan RT-PCR targeting the 5'-noncoding region of the human rhinovirus (HRV) genome. This is a one-step, real-time nucleic acid assay that offers rapid, sensitive, and quantitative results that are validated against all 100 recognized HRV prototype strains. This technology can be used to diagnose HRV, the most frequent cause of the common cold, and by labs studying HRV to further characterize the virus as a cause of the common cold or its role in more severe lower respiratory illnesses.

Inventors: Xiaoyan Lu, Dean D. Erdman
CDC Reference Number: I-027-07

Rift Valley Fever Virus

Development of Rift Valley Fever Virus Vaccines Utilizing Reverse Genetics

This invention allows for the generation of precisely defined attenuated vaccine constructs that contain complete deletions of critical virulence factors of Rift Valley Fever (RVF) virus. These attenuated vaccine constructs still have the ability to induce robust protective immunity following the administration of a single vaccine dose in a rat model of lethal disease. The vaccines can protect immunized animals against virulent virus challenge. The vaccine candidates also allow for the differentiation of naturally infected and vaccinated animals—a feature that is critical in agricultural settings. This approach will allow for the rapid generation of effective, safe RVF vaccine candidates to control and prevent the spread of wild-type RVF virus in a variety of settings, including preventing the infection of humans or animals during endemic, epidemic or epizootic situations in affected countries, or for prophylactic use among humans in high risk occupational settings, or following intentional release of RVF virus during bioterrorism.

Inventors: Brian Bird, Cesar Albarino, Amy Hartman, Bobbie Erickson, Thomas Ksiazek, Stuart Nichol.
CDC Reference Number: I-008-08
Publication Number: WO/2009/082647

Development of a Pan-Rift Valley Fever Virus Real-Time Quantitative RT-PCR Diagnostic Assay

Rift Valley fever (RVF) virus can cause severe illness in both humans and livestock. RVF is most common in eastern and southern Africa, although outbreaks have been reported in the Middle East and there is a threat of spread into Europe or the Americas. This invention describes a real-time RT-PCR assay for the detection of all known strains of RVF in humans or animals. This assay returns rapid, sensitive, and quantitative results, and can be used in the field for virus detection and surveillance.

Inventors: Brian H. Bird, Stuart T. Nichol
CDC Reference Number: I-005-07

Rotavirus

Novel Method to Inactivate Retrovirus

This invention describes a new method for inactivating a rotavirus while preserving the virus's proteins and antigenicity. Previous methods to inactivate the virus used formalin and beta-propiolactone, which were found to alter the rotavirus proteins and reduce its antigenicity. As a result, vaccines based upon these inactivated viruses were either partially or completely ineffective. This method accomplishes the same result while maintaining the virus's antigenicity for vaccination purposes. The invention also describes a method for vaccinating children against rotavirus diarrhea in both developed and developing countries.

Inventors: Baoming Jiang, Roger Glass, Jean-Francois Saluzzo
CDC Reference Number: I-010-06

Rotavirus Strain G9P11

Viral gastroenteritis is an acute diarrheal disease which can cause severe dehydration and complications, especially in young children. Rotaviruses are the single most important etiologic agents of viral gastroenteritis of infants and young children world-wide and cause 35-50% of hospitalizations for this condition during the first 2 years of life. This invention includes a modified rotavirus of the strain G9P11, and an isolated nucleic acid encoding the rotavirus of strain G9P11 and a purified antigen specific for the rotavirus which may be used to provide protection against rotaviral infection.

Inventors: Roger Glass, Bimal Das, Jon Gentsch, Maharaj Bhan
CDC Reference Number: E-122-94
Patent Number: 5,773,009

New Parenteral Human Rotavirus Vaccine Strains CDC-6, CDC-7, CDC-8, and CDC-9

This invention describes methods for adapting and producing human rotavirus vaccine strains to serve as an alternative to live oral rotavirus vaccinations and can prevent or control severe rotavirus diarrhea among children worldwide. These strains are produced in Vero cells, and the four new parenteral human rotavirus vaccine strains covered by this invention are representatives of common rotavirus serotypes. The vaccine can encompass a single serotype or multiple serotypes and can be administered alone or with other vaccines.

Inventors: Baoming Jiang, Roger Glass, Jon Gentsch
CDC Reference Number: I-011-06

New Human Rotavirus Vaccine Strains - CDC-66 and CDC-81

The invention describes methods for adapting and producing human rotavirus vaccine strains to serve as an alternative to live oral rotavirus vaccinations and can prevent severe rotavirus diarrhea among children worldwide. The two new parenteral human rotavirus vaccine strains covered by this invention are representatives of common rotavirus serotypes. The vaccine can encompass a single serotype or multiple serotypes and can be administered alone or with other vaccines.

Inventors: Baoming Jiang, Roger Glass, Yuhuan Wang
CDC Reference Number: I-012-06

Rubella Virus

Three Primer Real-Time RT-PCR Assay for Detection of Rubella Virus RNA in Clinical Samples

The Rubella virus is the cause of congenital rubella syndrome. This assay improves the ability to detect and diagnose rubella virus infections. The assay was developed to detect all known genotypes of rubella virus RNA in clinical samples. In this assay, a 3 primer system is used for the detection of both Clade 1 and Clade 2 rubella viruses. This invention eliminates the need for a second primer set for detection of Clade 2 viruses, and is therefore, more economical than the standard method of using 2 primers.

Inventors: Emily Abernathy, Dr. Joseph Icenogle, HaoQiang Zheng
CDC Reference Number: I-021-10

SARS

Real-Time TaqMan RT-PCR for Human Coronaviruses 229E, OC43, NL62, and HKU1

These four human coronaviruses are associated with a range of respiratory symptoms including high-morbidity outcomes such as bronchiolitis and pneumonia. An NL63 outbreak occurred in France in 2005, and an outbreak of OC43 occurred in British Columbia in 2003. Human coronavirus 229E has been recognized as a potential agent of nosocomial viral respiratory infections (NRVI) in high-risk infants. This invention includes real-time RT-PCR assays that were developed for detection of human coronavirus genomic RNA in clinical specimens. The invention is unique in that its sensitivity and specificty allows it to detect and distinguish all four currently recognized human coronavirus types.

Inventors: Dean Erdman, Ryan Dare
CDC Reference Number: I-019-10

Novel Coronavirus Isolated from Humans

This invention describes a human coronavirus, termed SARS-CoV, that has been identified as the causative agent of severe acute respiratory syndrome (SARS). The nucleic acid sequence of the SARS-CoV genome and the amino acid sequences of the SARS-CoV open reading frames are provided. This information could be used to prepare antibodies, in nucleic acid based methods of detection and diagnosis of SARS-CoV infection, or in pharmaceuticals for the inhibition or treatment of SARS.

Inventors: Thomas G. Ksiazek, et. al.
CDC Reference Number: I-018-03
Patent Number: 7,220,852

West Nile Virus

Humanized Murine Monoclonal Antibodies for Arboviral Serodiagnosis

This invention concerns human/mouse “chimeric” antibodies that are broadly cross-reactive with all flaviviruses or all alphaviruses. Two mouse monoclonal antibodies, one that is broadly cross-reactive with all flaviviruses and one that is broadly cross-reactive with all alphaviruses, have been modified using recombinant DNA technology, resulting in chimeric antibodies that are about 80% human and 20% mouse. These antibodies perform as human antibodies and can be used as positive control or “calibrator” antibodies of known specificity in diagnostic assays.

Inventors: John T. Roehrig, Brett A. Thibodeaux
CDC Reference Number: I-057-06

Duplex Microsphere Based Immunoassay for Detection of Anti-West Nile Virus and Anti-St. Louis Encephalitis Virus, Immunoglobin M. Antibodies, and Development of Software

This assay uses microspheres (Luminex Corp.) as a platform for a diagnostic assay that can concurrently detect immunoglobulin M antibodies to West Nile and St. Louis encephalitis viruses. Since this new technique is more efficient and uses an existing platform, it can be easily incorporated into current state and health department diagnostic testing for these viral antibodies. The method is particularly unique because data transformation and analysis software is an integral part of the test which allows a single result to be generated that can be compared back to the original large data set used in development. Thus, results from different laboratories can be directly compared to one another, if the same controls are used.

Inventors: Alison J. Johnson, Bradley J. Biggerstaff
CDC Reference Number: I-032-04
Publication Number: 20060188982

LICENSING INFORMATION

New biotechnology licensing opportunities are constantly being added to CDC's portfolio so be sure to visit our website often: www.cdc.gov/tto.

A blank Confidential Disclosure Agreement can be found on the last page of this brochure. Other forms are available upon request or can be obtained from the CDC website.

In addition, many other occupational safety licensing opportunities not included in this biotechnology brochure are available from CDC's Technology Transfer Office.

Questions about any of CDC's technologies may be directed to Suzanne Seavello Shope, JD, Technology Licensing and Marketing Scientist, 770-488-8600 or SShope@cdc.gov or Donald Prather, PhD, Scientific Marketing Specialist, 770-488-8612 or DMPrather@cdc.gov.

TECHNOLOGY TRANSFER OFFICE

In 1986, Congress passed the Federal Technology Transfer Act (FTTA) to improve the link between the federal laboratories' technology base and U.S. businesses. This law and related legislation authorized federal laboratories to patent and license inventions to businesses, and to collaborate with commercial firms on research and development projects. These activities benefit the public by transferring scientific expertise and technology from government laboratories, thereby encouraging the development of improved health care products, processes, and services.

The Centers for Disease Control and Prevention (CDC) established a Technology Transfer Office (TTO) to implement the FTTA and related legislation, and to facilitate access to CDC's world renowned scientists, engineers and state of the art laboratories. The TTO manages CDC's and the Agency for Toxic Substances and Disease Registry's (ATSDR) intellectual property by administering technology transfer activities related to patents, trademarks, copyrights, trade secrets, licenses, biological materials licensing agreements (BMLAs) and cooperative research and development agreements (CRADAs) with the private sector and academia.

CDC's technology varies from discovery and early stage inventions, to commercially ready products. There are hundreds of partnering opportunities available to domestic and international corporations through the CRADA process. To learn more about CDC, please visit our web site at www.cdc.gov. You can also learn more about the technology transfer process at CDC by visiting the TTO web site: www.cdc.gov/tto.

The enclosed abstracts of CDC's patents and patent applications represent research and development activities from CDC's Centers, Institutes, and Offices:

- Center for Global Health
- National Institute for Occupational Safety and Health
- Office of Infectious Diseases
  - National Center for Immunization and Respiratory Diseases
  - National Center for Emerging and Zoonotic Infectious Diseases
  - National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
- Office of Noncommunicable Diseases, Injury and Environmental Health
  - National Center on Birth Defects and Developmental Disabilities
  - National Center for Chronic Disease Prevention and Health Promotion
  - National Center for Environmental Health/Agency for Toxic Substances and Disease Registry
  - National Center for Injury Prevention and Control
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CONFIDENTIAL DISCLOSURE AGREEMENT

This Agreement is made by and between the Public Health Service ("PHS") and the company indicated below (hereinafter "Company").

In consideration of receiving for review from PHS a copy of the U.S. Patent Application(s) bearing the serial number(s) and title(s) indicated below (hereinafter "Application(s)"), Company agrees as follows:

1. Company agrees not to disclose any portion of the Application(s) to any third party without prior written permission from PHS, shall use reasonable care to maintain the confidentiality of the Application(s) with at least the same degree of care as is exercised in respect of Company's own proprietary information, and shall disclose the Application (s) only to those of Company's employees who have a need to review the Application(s) for the purposes specified in paragraph 4 below.

2. The following information categories are excluded from the confidentiality obligation of Paragraph 1:
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3. This Agreement does not grant any license rights under the Application(s).

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UNDERSTOOD AND ACCEPTED BY COMPANY:

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BY: _____ Mailing Address: _____
Authorized Signature

_____ _____
Typed or Printed Name and Title

_____ _____
Date

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APPLICATION FOR LICENSE TO PUBLIC HEALTH SERVICE INVENTIONS

Thank you for your interest in the technology transfer activities of the U.S. Public Health Service. Your answers to t he following questions will provide the foundation for licensing decisions. Please return this form and the required attachments to:

Technology Transfer Office
Centers for Disease Control and Prevention
4770 Buford Hwy
Mailstop K79
Atlanta, GA 30341

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U.S. Patent Application(s) Serial Number(s), Filing Date(s), and Patent Number(s) (if issued):

Title of Patent Application(s):

Biological Material(s):

Inventor(s):

Source from which you learned of availability of a license to the present invention(s):

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ON *SEPARATE ATTACHMENTS* TO THIS APPLICATION, PLEASE PROVIDE THE FOLLOWING INFORMATION:

I. DESCRIPTION OF APPLICANT

Include nature and type of applicant's business; number of employees; corporate/divisional commitment to R&D, production, sales & marketing; financial resources; products or services successfully commercialized and any unique capabilities of your company relative to the licensed technology. (If a prior license application has been submitted to the Technology Transfer Office within the past year, you may reference that application for the company description.)

II. OTHER LICENSES AND USE OF THE INVENTION

Identify any licenses previously granted to the Applicant under federally owned invent ion s. Also, identify, to the best of Applicant's know ledge, the extent to which the invention for which a license is sought is being practiced by private industry or Government, or is otherwise available commercially.

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Include definitions of licensed products, processes or methods; geographic territories; duration of license; claims (if known) of patent /patent application under which the proposed licensed technology would fall; and other terms for which you wish to make a proposal at this time.

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Include description of product(s) or method(s) to be developed with the licensed technology and, for each product or method to be developed, a description of expected product research and development programs, including (where relevant) major preclinical, clinical, regulatory, manufacturing and marketing stages; monetary and personnel commitments for each development stage; and the projected time to accomplish each stage of commercial development. *If you will be using the licensed technology in house but will not be directly commercializing the licensed technology or providing a service based on the technology, you need only describe the research program in which the licensed technology will be utilized.*

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Include relevant market segment (s) the licensed technology will serve when commercialized; market size and projected growth of relevant markets during the duration of the license; estimated market share once product is introduced; and sales projections based on market share analysis. *(THIS INFORMATION NEED NOT BE PROVIDED IN APPLICATIONS FOR COMMERCIAL EVALUATION LICENSES OR NONEXCLUSIVE COMMERCIAL RESEARCH LICENSES.)*

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A detailed statement as to *1)* why Federal and public interests will be best served b y exclusive licensing of this invention; *2)* why expeditious practical application of the invention is unlikely to occur under a nonexclusive license; *3)* why the exclusive licensing of this invention is a reasonable and necessary incentive to attract investments of risk capital; *4)* why the exclusive licensing of this invention will not tend substantially to lessen competition or result in undue market concentration; and *5)* why the proposed license terms and scope of exclusivity are not greater than reasonably necessary.

I certify, to the best of my knowledge, that all of the information provided on this application and on attachments to this application is true and accurate.

_____ _____

Signature of Applicant or Authorized Representative Date

_____

Print Name and Title

The commercial and financial responses in this application will be treated as privileged and confidential information as provided in 15 U.S.C. 209(a); and, to the extent permitted by law, will not be accessible under the Freedom of Information Act.